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Radiotherapy in Advanced and Incurable Malignant Disease[1]

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I consented to participate in this symposium on the management of the patient with advanced or incurable cancer if I might be allowed to preach a small sermon rather than make a formal presentation. This is because I believe that the management of a patient with a malignant disease from which he is not going to get well —or has little likelihood of getting well— is at least as much a matter of point of view and plan of action as it is a matter of technic and end-result, perhaps more. I shall not discuss in detail indications and conditions in which radiotherapy is useful. This we all know or it is available to us in standard texts. I should rather approach this from the standpoint of general principles.

Oliver Wendell Holmes is quoted as saying that, while one of the physician's functions is to assist in the coming in, another is to assist in the going out. A radiologist has ordinarily little to do with man's coming in, but he often can have much to do with his going out, especially when the going out is the long and painful process which it sometimes is in the case of advanced and incurable malignant disease. This is the role of what is called palliative radiotherapy.

Some of you no doubt heard Dr. Ralston Paterson talk on this subject in Mexico City last summer in a symposium similar to this. I have been tempted just to read his essay to you and forget what I have written. I could do no better. Though I have not done this, I hope that I will be forgiven if some of you recognize what may sound like a few cribs from his admirable paper.

Radiotherapy of malignant disease has two roles, the first—and by far the most important—is its role as a principal means of control and cure of cancer. Of this we must never lose sight. The notion prevalent in some places that radiotherapy is of value only to the incurable patient and that "to cure means to cut" is, of course, only a reflection of inadequate experience in the management of malignant disease. There is a growing tendency for this phase of radiotherapy to be carried out in places where advantage can be taken of concentration of experience and availability of the rather vast array of equipment and facilities which modern radiotherapy requires and which for economic reasons is not to be had in every community. With this trend, I am heartily in accord.

The other scarcely less important role lies in the management of the patient with malignant disease from which he is not likely to recover, either because of the nature of the disease, as, for example, the malignant lymphomas and cancer of the lung, or because of the degree of its ad-

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vancement, as in cancer of the breast with metastases and Stage IV carcinoma of the cervix.

The assumption of this role is no mean part of the radiologist's activity, and I believe that it must continue to be the concern of every radiologist, whether or not he deals with curable cancer in a definitive way. Palliative radiotherapy does not require an elaborate and expensive array of facilities, and it must remain available to patients close to their homes. Much more important than fancy equipment is the desire to help, an understanding of the disease, a knowledge of what can and cannot be offered by radiotherapy, and a thorough appreciation of certain general principles. It is these general principles of procedure of which I should now like to speak. If this is done in a somewhat arbitrary fashion, it is for want of time and not for want of recognition of room for differences.

The first of these pet principles of mine is to the effect that it is the purpose of palliative radiotherapy to provide symptomatic relief. This means that the patient must have something wrong of which he can be relieved. The mere fact that he has a malignant disease and that it is of an incurable nature or stage of advancement is not always justification for proceeding with radiotherapy or, for that matter, for doing anything. What benefit is gained by disturbing the patient with a course of radiotherapy intended to relieve symptoms which he doesn't as yet have? This is especially true in the very young and in the elderly. There are, of course, times when, by action in the absence of symptoms, radiotherapy can be used to prevent symptoms which the experienced physician knows will come, but all too often such so-called palliative treatment is meddlesome and does little more than disturb the equanimity of the patient.

A primary purpose of radiotherapy is also to prolong life and put off the day of dissolution, and in this it is often successful as in the instance of malignant lymphomas involving vital parts. To this end no effort should be spared. Prolongation of life, however, if it is to be worthwhile, must mean the prolongation of a useful and a comfortable existence, with relief of symptoms and restoration to some degree of health and happiness. The mere adding of days cannot be justified if they are to be days of misery and pain, with nothing to look forward to other than an end, which without so-called palliative therapy would have come mercifully sooner. We must with absolute certainty realize the truth of Lord Horder's observation that the duty of the physician is to prolong life, but it is not his duty to prolong the act of dying.

When a course of palliative radiotherapy is entered upon, we must have reasonable assurance that the relief sought by the patient and offered by the physician will materialize. Radiation is not effective in all neoplastic conditions nor in all situations. The circumstances under which it will be successful are by now quite well known. The day of empiricism has long since passed and the formula, "If at first you don't succeed, try, try, again," admirable as it may be as an admonition to our youngsters, has no place in radiotherapy. The neoplasm must, in some part at least, be susceptible to ionizing rays. To persist in treatment of conditions known not to be amenable to relief by x-rays, brings discredit to a useful agent and is a waste of the patient's resources, though there are, of course, extraordinary times when radiotherapy can and will be used even though the chances of securing relief are almost nil. Then all parties, with the possible exception of the patient, must understand perfectly what is being done.

If palliative radiotherapy is offered, we must be as sure as we can that palliation is all there is to be had and that we are not denying the patient the chance of cure of his disease by radiotherapy or by any other method.

Failure to approach a still curable situation in a manner likely to produce a cure, assuming the attitude of "the poor fellow has cancer, let's just make his last few days

more comfortable" is even worse than to persist in curative efforts to the general detriment of the patient when obviously he can no longer be rescued.

Palliative radiotherapy should not be so vigorous or so prolonged as to add to the patient's burden or to occupy an undue portion of his days yet remaining. If relief can be obtained by a short course of therapy, it makes no sense to continue treatment beyond the time when relief may be anticipated. The dose of radiation should still be sufficient, however, to give respite which has promise of being reasonably prolonged. It does no good to give such a small dose of radiation that symptoms return after the briefest period. Neither is it good palliation to give a course of radiation approaching that which would be considered of curative intent.

When attempting palliation, we must be sure that it will not make an already bad matter worse. Radiotherapy inadvisedly persisted in can result in adding necrosis to disease. Even if there has been no previous treatment, there are times when all it does is to permit the patient to die of a more miserable development of his disease than the one nature had planned. Relief of urinary obstruction for example in a patient with advanced cancer of the cervix, where nature with considerable wisdom has already provided an excellent anesthesia in the form of an elevated urinary nitrogen, is no kindness when it means only that the patient must then die later, more aware of her pain, her infection, and her uncontrolled local disease.

There is a time in the going-out process when radiotherapy no longer has anything to offer and may even accelerate the act of dying. This is the most difficult situation to recognize. This is the place where the more experienced physician, who sees patients and not merely records, has a real advantage. When this time comes, it is just as important to provide comfort by other means and not to molest the patient with radiotherapy as it was formerly to provide respite by irradiation. The overworked family physician, under pressure of the desperate family or an ambitious but inexperienced house officer, at times is faced with the plea that we must do something or the patient will shortly die. I know of only one situation in which a patient *in extremis* may sometimes be rescued by radiotherapy. That is when he is suffocating because of severe upper mediastinal obstruction. When this is due to a highly radiosensitive tumor, radiotherapy in conjunction with nitrogen mustard or some similar agent often provides dramatic respite. This is an exception to the rule, and the hope that radiotherapy may in some mystical way change the course of the patient dying of overwhelming malignant disease is a vain one.

The patient must be in a position to enjoy whatever palliation may be expected. His expectancy must at least exceed the latent period between therapy and relief. Finally, we as physicians must never deny the right of man to die as well as to live. I am afraid that in our urge to help we sometimes substitute our wills for the patient's and by so doing make his last days miserable, pestering him with a display of more science than sense.

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REFERENCES

PATERSON, R.: Use and Abuse of Palliative Radiotherapy. J. Faculty Radiologists **8:** 235–238, April 1957.

A New Way of Dying. Atlantic Monthly **199:** 53–55, January 1957.

Editorial: Life-in-Death. New England J. Med. **256:** 760–761, April 18, 1957.

(*Pro le summario in interlingua, vider le pagina 329*)

Complications of Advanced Cervical Cancer and Their Management[1]

HERBERT E. SCHMITZ, M.D., Sc.D., F.A.C.S., and JOHN H. ISAACS, M.D.

THE EMPHASIS in cancer today is upon early diagnosis and adequate therapy. This crusade has been effective. More and more cases are being found in their early stages, with a resultant increase in salvage rate. Unfortunately this enthusiasm has been at the expense of the far advanced, apparently hopeless case. In reviewing the literature on terminal cancer care, one finds little discussion of the practical solutions to the problem. With this in mind, the cervix cancer deaths at the Mercy Hospital Institute of Radiation Therapy, from 1933 through 1955, were reviewed. These numbered 350. Some of these patients received their primary treatment at the Radiation Institute, while others were referred after previous therapy elsewhere had failed. During this twenty-three year period there was a constant improvement in the care of the terminal patient. Not all the cases received palliative therapy, but most of them did. The realization that life expectancy of the patient with an average Stage IV lesion is thirteen months reminds us that palliation is no small part of cancer therapy. Its purpose is to furnish a reprieve from the agonies of the disease. Prolongation of life is not its measure. Should life be prolonged, the coincidence may be considered fortuitous.

Craver and Finkbeiner (1) warn us of the vagaries of the natural history of cancer with its alternating periods of growth and quiescence. By utilizing all the surgical, radiotherapeutic, and chemotherapeutic technics available, we can give the patient relief and in many instances retard tumor growth. It has been possible, as a result of a thorough study of these 350 cancer deaths, to set down certain criteria for the management of the terminal case as practiced in our own clinic. In such a study one fact becomes apparent almost at once, namely, that the physician must treat the entire patient and not only the afflicted organ. The major problems encountered included pain, vaginal hemorrhage, enterovaginal, rectovaginal, and vesico- or ureterovaginal fistulas, uremia, malnutrition, anemia, mental depression and despair.

TABLE I: SECONDARY RADIOTHERAPY IN 187 CASES OF CERVICAL CANCER

Type of Patient	No. of Cases
Adequately treated primarily	106
Inadequately treated primarily	81
TOTAL	187
Type of Irradiation	
One palliative x-ray course	125
Two or more palliative x-ray courses	28
Palliative irradiation with radium	10
Combined palliative therapy	24
Irradiation to distant metastases	8

Pain is a major problem but one that should not be solved by immediate around-the-clock narcotic administration. The mechanism of pain production by cancer includes the compression and destruction of nerves, invasion of contiguous pain-sensitive structures, infiltration and occlusion of arteries, veins and lymphatics, infection and inflammation, and obstruction of hollow viscera. The most effective means of combating these complications has been palliative irradiation. Phillips (4) reported 72 cases of cancer of the cervix treated with palliative irradiation at Memorial Hospital in New York. Seventy per cent of his patients received symptomatic relief and 8 per cent of those with Stage IV disease survived five years. In our clinic, 187 patients received secondary irradiation with 1,000-kv x-rays or radium or a

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TABLE II: PROCEDURES FOR INTERRUPTION OF PAIN PATHWAYS

	No. of Patients
Subarachnoid alcohol injection	22
Chordotomy	7
Lobotomy	1
TOTAL	30

combination of both. The type of irradiation employed is shown in Table I.

The irradiation is given on an empiric basis and changes in the size of the irradiated tumor are carefully observed. The relief of pain and, in some instances, reduction in size of an extremity which had been edematous have been dramatic. Although this paper is not concerned with the five-year survival rate in such cases, it should be mentioned that some patients so treated have lived well beyond the five-year interval. Of the 187 patients who ultimately died of cancer, the length of life following irradiation varied from one to forty-eight months. The average survival was 11.6 months.

Those patients not benefited by irradiation therapy may be relieved by other means. It is not unusual for pain to be produced by accompanying infection rather than cancer itself. If such a diagnosis can be established, antibiotics are the treatment of choice.

Extensive palliative operations were carried out in 28 cases. In some of these immediate postoperative deaths occurred, but in most instances the unbearable symptoms associated with fistulae were eliminated and life was prolonged. The average survival following surgery was nine and one-half months. For the young woman with children such a prolongation of life affords an opportunity to spend a little more precious time with her family. Some surgical cases (not tabulated here) have gone beyond the five-year mark of survival.

When irradiation is either contraindicated or ineffective and radical surgery unwise, the physician must consider means of interrupting pain pathways by either neurosurgical or chemical measures. Of prime importance in applying these technics is the fact that the pain must be localized to an area that may be effectively rendered analgesic by interruption of its nerve supply without producing a deficit which may be more disabling or detrimental than the pain itself. Such measures should be utilized as early as possible and not as a last resort when the patient is so close to death that the risks involved are not only palpable but the advantages imperceptible.

The neurolytic agent most frequently employed in our clinic is absolute alcohol to produce a subarachnoid block. This will, if accurately deposited, give relief for weeks or months, especially of the severe hip and lower extremity pain encountered with cervical cancer. Technically such neurolytic agents are somewhat difficult to administer, since only a very small volume may be injected if complications are to be avoided, and the needle must be precisely placed if a block is to be achieved.

A more exact method for producing regional analgesia is transection of the anterolateral quadrant (chordotomy) of the spinal cord. There is usually concern on the part of the layman, and the physician as well, that such an attack will greatly limit the motor function of the part. This complication, however, is seldom encountered in the hands of a competent neurosurgeon. The patient with unilateral pain in the hip or lower extremity is the ideal candidate for such an operation. Loss of motor function in the extremity or of the sphincter power is infrequently encountered. Houde (2) in a recent publication on pain and the cancer patient reports favorable results following this procedure.

Frontal lobotomy has been successfully employed by some, but our experience has been disappointing. The frequent personality change without remarkable improvement in the pain reaction seems reason enough to avoid such a procedure except in the very rare case.

All of the methods mentioned have been employed in our clinic, as shown in Table II. Our most satisfactory results have

been obtained with alcohol injections. Lack of enthusiasm for chordotomy is not based on the study of cervical cancer alone but on the results observed in all pelvic cancers so managed.

Aside from the use of palliative irradiation or the blocking of nerve pathways, judicious use of analgesics will afford the patient adequate relief for many weeks before one must resort to morphine. Aspirin (5), administered in doses of 15 grains, will raise the threshold of pain about 35 per cent. Phenacetin (frequently shunned because of its toxicity) is often helpful, especially in those whose life expectancy is short. When such drugs become ineffective they may be used in combination with small doses of codeine. Ultimately one may have to resort to morphine but its use has not been extensive in our series. Not only does its effectiveness diminish with prolonged use, but addiction can pose a greater problem in management than the cancer itself. When morphine is used, careful attention to the bowels is necessary to avoid constipation and fecal impaction. Drug addiction in an already malnourished patient with flagging appetite only serves to hasten an ultimate demise.

In addition to the analgesics and narcotics, other drugs are available to either complement or enhance the effect of those being used. Cobra venom will sometimes provide prolonged periods of relief. It has a cumulative effect and should be used at least thirty days before it is considered ineffective. Whether chlorpromazine will actually be effective in cancer patients as a potentiating agent to the narcotics is still not definitely established.

Profound vaginal hemorrhage, which may occur sporadically and produce severe anemia or even death, must be prevented. With the frequent use of palliative irradiation, hemorrhage has not been a frequent complication in our clinic but it has been necessary to employ bilateral hypogastric artery ligation on 8 of our patients. This will unquestionably stop the hemorrhage or appreciably reduce it. The extraperitoneal approach is preferred. Bilateral incisions are made in the lower abdominal quadrants and the peritoneum is gently separated medially until the iliac vessels are exposed. The procedure is not traumatic and the postoperative complications are few and of minor importance. Cutting off the iliac and ovarian blood supply to the cancer results in a regression in its growth.

Malodorous vaginal discharge is another source of discomfort and a cause for neglect on the part of friends and relatives. A practice suggested over forty years ago by the gynecologists of that day is still useful for reducing the odor but unfortunately is little used today. It consists in application of an acetone pack to the cervix. This can be accomplished as a simple home or hospital procedure with no discomfort to the patient. If the outer two thirds of the vagina are coated with vaseline and a solid vaginal speculum is inserted, so that only the necrotic growth is exposed, small acetone saturated cotton sponges can be introduced, causing the necrotic tissue to be dissolved. In such instances both the patient and her family are grateful for periodic relief from the sickening odor. Usually one application every twenty-four or forty-eight hours is sufficient to insure freedom from odor and leukorrhea, and will serve to minimize vulvar excoriations.

Uremia and/or pyelonephritis may be a cause of death when proper management would have prevented their occurrence. Since the ureter passes just lateral to the cervix in its course to the bladder, the invading cancer gradually compresses it, producing hydronephrosis with ensuing uremia and pyelonephritis. Intravenous pyelograms will confirm the presence of this complication. In the poor risk patient, cystoscopic examination with the passage of ureteral dilators will often allow improved kidney function for a variable period of time. Even the fibrosis from irradiation or surgical intervention may be the cause of constriction and can be alleviated by dilatation.

Ultimately the urinary bladder is invaded, with resultant vesicovaginal fistula. In such an event the patient is immediately restricted in her activity. The constant dripping of urine over the perineum demands correction. The diversion of the urinary stream presents many problems to the gynecologic surgeon. He must prevent upper urinary tract infection, maintain electrolyte balance, and provide a practical means for the patient to care for herself. If the disease has not invaded the posterior aspect of the pelvis, ureteral transplants provide a means of maintaining urinary continence *via* the rectal sphincter. The great danger following such surgery is massive kidney infection and death. One of our patients who had a successful total pelvic exenteration with a wet colostomy was free of disease but died a little over a year postoperatively of a urinary tract infection not actively treated.

One method which may prove more satisfactory in preventing urinary tract infection following ureteral transplant is that suggested by Parsons (3). He has employed a left transverse colostomy above the ureterosigmoid anastomosis. The entire sigmoid and rectum are utilized for the collection of urine. If the patient is in good physical condition, the use of the Bricker pouch may be considered. This method, in which an isolated loop of ileum is used as an artificial bladder, reduces the danger of electrolyte imbalance and infection, but continence is lost and the patient must use a Rutzen bag. Our experience with the Gilchrist pouch has been somewhat disappointing, since the procedure has had a fairly high mortality in our hands. Cutaneous ureterostomies are definitely unsatisfactory. They are difficult for the patient to manage and, in addition, the os tends to become stenotic and bouts of pyelitis are frequent.

In conjunction with vesicovaginal fistulas, the rectum is often invaded and breaks down, discharging the fecal stream into the vagina. Such patients, if their life expectancy is of any length, deserve operative repair. We have had several cases where such a situation existed and have repaired the fistulas satisfactorily. Since the bladder floor is destroyed and empties into the vagina, and the fistula into the rectum is quite large, the entire bladder, vagina, and lower rectum may be used as a urinary reservoir. First the fecal stream is deviated by means of colostomy. The lower third of the vagina is then closed so that in effect the urine drains from the bladder into the vagina and then into the rectum, with utilization of the rectal sphincter to retain continence. Such a diversion demands little actual surgical manipulation. Closure of the vagina requires no more time than a perineorrhaphy, and the colostomy may be done as a simple double-barrel procedure prior to the vaginal surgery. Liberal use of sodium acid phosphate by mouth prevents the formation of urinary calculi. The cases with urinary tract complications and the methods of palliation are listed in Table III.

TABLE III: PALLIATIVE MEASURES FOR URINARY TRACT COMPLICATIONS

	No. of Cases
Uretero-sigmoid anastomosis	7
Skin ureterostomies	4
Transurethral resection of obstructing tumor	1
Bladder fulguration	2
Urethral dilatation	2
Ureteral dilatation	3
Nephrectomy	5
Nephrostomy	1
Uretero-entero-vesical anastomosis	1
TOTAL	27

When the rectum becomes involved, causing either fistula or obstruction, colostomy is the best means of control. This was required as a separate operative procedure in 12 of our patients. Proper instructions must be given the patient with a colostomy. Aspirin taken in doses of 10 to 20 grains, with as little water as possible, will often check an exacerbation of diarrhea. For the definitely overactive bowel, methylcellulose taken with a minimum of water is best. Methylcellulose also has the property of practically eliminating the fecal odor.

Those patients who have received ade-

quate irradiation may suffer small bowel damage with resultant fistula or necrosis. Such a situation, when neglected, may cause death or prolonged disability even though there is no cancer tissue remaining. Small bowel roentgen studies may be helpful, but a definite diagnosis may have to be made at the time of laparotomy. The involved areas of bowel, when discovered, may be resected, with anastomosis. This was carried out in 5 instances in our series.

Finally we come to a phase in the care of the terminal cancer patient, which requires more art and understanding on the part of the physician than any of the technical procedures discussed. Whether or not the patient is aware of the scientific diagnosis, she is always aware of her situation. Such knowledge invariably causes mental depression, anxiety, and anorexia with final cachexia. The physician should never consider the plight of his incurable cancer patient a hopeless one. She deserves the same meticulous attention that the incurable cardiac or hypertensive patient enjoys. Whether she is at home or in the hospital, proper nutrition will do a great deal to fortify the body against the ravages of her disease. The diet must be made both wholesome and appetizing. A member of the family or a conscientious nurse must be present for meals to stimulate morose spirits and poor appetite. Anemia and avitaminosis, which invariably accompany cancer, can be controlled with blood transfusions, vitamins, iron, and liver supplements. Even the early cases with an optimistic prognosis will not respond unless adequate nutrition is maintained. Of equal importance is the maintenance of near normal activity. We are all familiar with the elderly patient with a fractured hip who, if allowed to remain at bed rest, will degenerate rapidly and die. Cancer patients must have all the encouragement possible.

Most important of all is the patient's morale which can be bolstered by her doctor. Daily visits to the terminal hospital patient will brighten her day; a simple change in diet or deviation from the routine medication will give her the feeling that she is not neglected—that her doctor will not forsake her. The courage such interest fosters far exceeds the benefit any analgesic preparation can afford.

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REFERENCES

1. CRAVER, L. F., AND FINKBEINER, J. A.: Long-Term Survivals in Cancer. M. Clin. North America, pp. 673–686, May 1956.
2. HOUDE, R. W.: Pain and the Patient with Cancer. M. Clin. North America, pp. 687–703, May 1956.
3. PARSONS, L., AND TAYMOR, M.: Longevity Following Pelvic Exenteration for Carcinoma of Cervix. Am. J. Obst. & Gynec. **70**: 774–785, October 1955.
4. PHILLIPS, R.: Principles and Results of Palliative Radiotherapy in Nonresectable Cancer. M. Clin. North America, pp. 807–820, May 1956.
5. Comfort in Terminal Care. Cancer Bull. (Texas) **7**: 117–119, November-December 1955.

SUMMARIO IN INTERLINGUA

Complicationes de Avantiate Cancere Cervical e Lor Tractamento

Le major problemas in le tractamento de patientes con multo avantiate cancere cervical es dolor, hemorrhagia vaginal, fistulas enterovaginal e vesico- o ureterovaginal, uremia, malnutrition, anemia, depression mental, e despero.

Le dolor suffrite per le patiente de cancere cervical pote esser le effecto de compression e destruction de nervos; de invasion de structuras contigue; de infiltration e occlusion de arterias, venas, e vasos lymphatic; de infection e inflammation; e de obstruction de visceres cave. Le plus efficace medio pro combatter iste complicationes es irradiation. In le clinica del autor, 187 patientes qui moriva subsequentemente ab cancere recipeva irradiation palliative de 1.000 kv in le forma de radios roentgen o radium o ambes. Le alleviamento del dolor e in certe casos le reduction del dimensiones de un extremitate edematose esseva dramatic. Le super-

viventia medie in iste gruppo esseva 11,6 menses. Un certe numero de patientes viveva un considerabile periodo ultra le limite de cinque annos, sed le presente articulo concerne solmente illes qui moriva ab cancere.

Chirurgia palliative esseva effectuate in 28 casos, resultante in un superviventia medie post le operation de nove menses e medie. In plus, le interruption del dolorifere circuitos esseva effectuate per methodos como le injection de alcohol (pro producer blocage subarachnoide) e chordotomia. Lobotomia frontal non se monstrava satisfactori pro iste objectivo.

Altere mesuras mentionate include therapia a antibioticos—specialmente quando le dolor es causate per infection; le uso de analgesicos e de altere drogas que promove lor effecto; ligation bilateral del arteria hypogastric pro arrestar le hemorrhagia; application de compressas acetonic al cervice pro combatter le odor repugnante del discarga vaginal; colostomia pro evitar implication del recto; e resection chirurgic in caso de lesiones radiational in le intestino tenue.

A parte iste mesuras specific, mantenentia de un nutrition adequate, correction de anemia e avitaminosis, e attention al moral del patiente es del prime importantia in le effortio de prolongar le vita del patiente de cancer sub conditiones de conforto al minus relative.

SUMMARIO IN INTERLINGUA

Radiotherapia in Avantiate e Incurabile Casos de Morbo Maligne

(*Pagina 321*)

Le thema de radiotherapia pro cancere avantiate es considerate in le presente articulo ab le puncto de vista de principios general plus tosto que ab le puncto de vista de indicationes specific. Radiotherapia in morbo maligne ha duo functiones: (1) Illo es un medio cardinal de subjugation e cura, e (2) illo effectua palliation in casos in que recovramento es improbabile.

Le prime objectivo de irradiation palliative es le provision de alleviamento symptomatic. Un secunde objectivo primari es le prolongation del vita—providite que il pote tractar se del prolongation de un existentia utile e confortabile—con le restauration de un certe grado de sanitate e felicitate. In tentar le effectuation de un resultato palliatori, le radiologo debe esser satis certe de successo, i.e. le neoplasma debe esser susceptibile—al minus in parte—al action de radios ionisante. In plus, le radiologo debe esser certe que palliation es le optimo a sperar e que le patiente non perde le chance de esser curate.

Le therapia palliative debe esser de natura a non augmentar le difficultates del patiente e a non occupar un portion excessive del tempore que es ancora le sue. Finalmente, le patiente qui ha ultrapassate le limites de palliation sperabile non debe esser molestate con mal-inspirate effortios a "continuar le lucta." On debe respectar le derecto human a morir e non solmente le derecto a viver.

The Present Status of Hormone Therapy in Advanced Breast Cancer[1]

B. J. KENNEDY, M.D.

DURING THE PAST decade, alteration of hormonal factors by the administration or deprivation of hormones has profoundly affected the growth rate of advanced carcinoma of the breast. The multiple means of changing the hormone status have made it imperative that a systematic approach to hormonal alteration be established in order that maximum benefit and maximum control of the disease may be obtained.

The modes of action of these changes in hormonal status are subtle. It has been demonstrated that the response of a tumor to hormone therapy is governed by the current endocrinologic status of the patient. This is determined in part by the menopausal age and not the chronological age. Selection of treatment of advanced breast cancer is based upon deprivation of those factors that maintain or accelerate tumor growth and administration of hormonal agents antagonistic to tumor growth. Six major measures are involved: (*a*) ovarian suppression, (*b*) adrenal suppression, (*c*) pituitary suppression, (*d*) androgenic hormone administration, (*e*) estrogenic hormone administration, and (*f*) adrenocortical hormone administration.

CASTRATION

The role of hormones in breast cancer was introduced in 1889, when Schinzinger proposed surgical castration (ovariectomy) as a rational therapeutic approach (1). This method of treatment was first employed by Beatson, who in 1896 reported improvement following castration in inoperable cases (2). Beatson's observations have since been confirmed by many investigators, and castration has become an accepted treatment for advanced mammary cancer. A wide disagreement exists, however, with respect to the optimum time for its performance.

Castration is primarily of value as a palliative procedure in patients with advanced primary, recurrent, or widespread cancer of the breast. The beneficial effects are essentially confined to the premenopausal period. Those improvements occasionally reported following castration a few years after spontaneous cessation of the menses demonstrate that in those years there is residual ovarian activity (3).

Castration results in relief of symptoms, objective regression of soft-tissue lesions, and calcification of osseous metastases. The data indicate that palliation is achieved in 20 to 50 per cent of premenopausal patients. The average duration of such improvement is approximately ten months, with a range from three months to five years (4). Attempts have been made to predict a favorable response and on this basis to select patients for castration. There is no correlation of the result with the histologic characteristics of the cancer. Patients with osseous metastases suffering increased bone pain in the premenstrual period are, however, prime candidates for castration, the exacerbation of pain being apparently due to stimulation of the cancer by ovarian hormones.

Both oophorectomy and irradiation have been employed as means of producing ablation of the ovaries. Surgery guarantees permanent eradication of ovarian hormone production. The efficacy of radiation is less certain. The development of

[1] From the Department of Medicine, University of Minnesota Medical School, Minneapolis, Minn. This investigation was supported in part by the American Cancer Society, by grant DRG-283B from the Damon Runyon Memorial Fund for Cancer Research, and by Research Grant CY-3143 from the National Cancer Institute, National Institutes of Health, U. S. Public Health Service.

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amenorrhea and postmenopausal symptoms is not a reliable indication of ovarian suppression. Even though the activity of the ovaries appears to cease completely following irradiation, functional recovery may occur, with reappearance of the menses. It is clear that the failure to suppress ovarian function completely and permanently by radiation is due in part to insufficient dosage. The "sterilizing" dose employed in the past is insufficient. Adequate irradiation may be as efficacious as ovariectomy, though this point remains to be clarified by further study. A tissue dose of 1,200 to 1,500 r to the ovaries delivered within a ten-day period should be attained. The effective dose level appears to be higher in younger women because of greater ovarian activity (3).

The degree of ovarian destruction can be judged by serial studies of the vaginal smear. Measurement of urinary estrogen excretion has not proved to be valid because of the inaccuracies of the chemical technics. Suppression of ovarian function following irradiation occurs only after a minimum of six to eight weeks following initiation of therapy. If a rapid castration effect is necessary because of acute or distressing complications (hypercalcemia, brain metastases), ovariectomy is undoubtedly preferable. In those patients too ill to tolerate anesthesia or a surgical procedure, concomitant androgenic hormone therapy may hasten the effect of irradiation in suppression of ovarian function.

Following castration in young women still menstruating, severe menopausal symptoms may occur. The usual hormonal management of this syndrome cannot be advised under these special circumstances. Since the prime purpose of ovarian ablation is the removal of estrogenic hormones, the therapeutic use of such agents is contraindicated. Nor can androgens be recommended in this situation, since it has been established that androgenic hormones are in part converted to estrogenic hormones (5), and accelerated growth of breast cancer has been reported in 10 per cent of patients with osseous metastases undergoing androgen therapy. When necessary, the management of menopausal symptoms consists primarily of sedation.

There is widespread disagreement as to whether prophylactic castration increases the curability rate when performed at the time of a radical mastectomy for cancer confined to the breast or regional lymph nodes. The poor results of surgical therapy in premenopausal patients, exacerbation by pregnancy and lactation of cancer growth, and the stimulating effect of exogenous estrogenic hormones are cited as reasons for recommending prophylactic castration. The solution of the problem rests upon accurate determination as to whether the procedure increases the period before the recurrence of metastases and whether it prolongs total survival time. The major difficulty in evaluating the situation is the lack of comparable series of prophylactic castrations, therapeutic castrations, and cases without castration.

Preliminary data from several investigators suggest that prophylactic castration prolongs the period before the onset of metastases (4). Furthermore, in smaller series, ovariectomy appears to be superior to radiation therapy. In many instances, however, the dose of radiation seems to have been inadequate. Unfortunately in these series the total survival times have not been reported.

No data are available comparing total survival time in patients receiving prophylactic irradiation with an equivalent group in which castration was postponed until metastases were manifest. It would appear that prophylactic surgical castration has a significant effect in delaying the onset of metastatic disease. To settle the disagreement as to whether prophylactic castration is superior to therapeutic castration, adequate analyses of comparable cases must be obtained in terms of total survival.

Since one must consider further hormonal therapy after the onset of metastases, it is advantageous to carry out castration as a therapeutic procedure in

Fig. 1. J. H. Recalcification of osteolytic metastases seventeen months after bilateral oophorectomy.

order to determine whether or not the tumor is ovarian-dependent. In this manner, decisions regarding further ablative procedures or hormonal administration are made less difficult. In view of this long-term concept of hormone therapy and the paucity of data regarding prophylactic castration, the dogmatic support of this latter procedure is not justified for the present.

Case Report

J. H., aged 42, had a left radical mastectomy in July 1954. A scirrhous carcinoma with involvement of one of thirteen axillary lymph nodes was found. An extension of the surgical procedure to a supra-radical mastectomy was carried out two months later. Examination of the supraclavicular nodes, internal mammary nodes, axillary nodes, and all other nodes removed showed them to be cancer-free. Following this, radiation therapy was carried out in the routine manner. In January 1955, the patient requested that a right simple mastectomy be done for cosmetic purposes. No cancer was present in that breast.

In June 1955, the patient began to suffer from back pain. Osseous metastases were present in the left ilium. Since the menstrual periods were regular, a bilateral oophorectomy was performed on June 20, followed by marked relief of pain. The patient was disturbed, however, by a severe postmenopausal syndrome consisting of flushing, nervousness, and arthralgia. Hormone therapy was contraindicated, and only sedatives were employed. Gradually the menopausal symptoms declined in severity. After four months, roentgenograms revealed recalcification of the osteolytic lesions in all areas (Fig. 1). The patient is free of pain and has no evidence of cancer on clinical examination two years later.

Comment: This case is representative of carcinoma of the breast in the premenstrual period. Despite radical definitive surgery for control of the disease, osseous metastases occurred within a year of the initial operation. These showed excellent regression following oophorectomy. This patient will be an ideal candidate for hypophysectomy when subsequent reactivation of the disease is manifest.

BILATERAL ADRENALECTOMY

It has been established that adrenal factors sustain or propagate certain breast cancers. Pathologic examination of patients previously castrated revealed enlargement of the adrenal glands in some instances. It has been postulated that this enlargement is a source of increased production of hormones stimulating the growth of the cancer. Women with cancer of the breast who have undergone ovariectomy continue to excrete estrogenic compounds in the urine (6). It is clear that the adrenal glands are capable of secreting hormones that sustain the growth of breast cancer.

From the numerous reports of bilateral adrenalectomy in advanced cancer of the breast, 400 cases have been culled for review. From these it is apparent that there is a definite dissociation between subjective and objective improvement, since approximately 65 per cent of the patients showed subjective improvement, while objective regression occurred in 34 per cent. In various individual series an incidence of objective regression of 40 to 45 per cent has been reported (6,7). It would appear that the rate of regression after bilateral adrenalectomy is similar to that following ovariectomy. In quality and type the regression has also resembled that recorded for castration and other hormone therapy. Its mean duration has been approximately nine months (8), although remissions of three years have occurred.

The benefits of adrenalectomy in women with advanced breast cancer are considered to be due primarily to the removal of another source of endogenous estrogenic hormone. Cancer of the breast dependent upon ovarian hormones should respond favorably to adrenalectomy. That it does so is substantiated by the available data. Patients failing to benefit from oophorectomy fail to respond to adrenalectomy. Knowledge of the response in a premenopausal patient to castration provides the best criterion for selection of the patient for removal of the adrenals.

The disadvantages of bilateral adrenalectomy are as follows: The patients are difficult to regulate postoperatively; the procedure is a major undertaking; because of the presence of accessory adrenal tissue removal of the source of hormone production may be incomplete.

HYPOPHYSECTOMY

That the pituitary gland is an important factor in the control of the growth of breast cancer is well established. In rats hypophysectomy definitely retards the growth of tumors (9), while the administration of growth hormone increases their incidence (10). This hormone appears, also, to have a stimulating effect on tumor growth in man. Its administration to two patients with advanced cancer of the breast produced an increase in calcium excretion, which is interpreted as a possible increase in the growth rate of the tumor (11, 12). It has been postulated that the ameliorative effects of massive doses of sex hormones in patients with breast cancer may be due to depression of pituitary function (13). It was inevitable, therefore, that eventual total surgical hypophysectomy would be performed.

The technic of hypophyseal ablation has varied. The operation requires the skill of an experienced neurosurgeon. A craniotomy is performed. Peyton carried out an excision of the anterior medial portion of the right frontal lobe, providing a wide exposure of the sella turcica (14). Ray retracts the frontal lobe (15). The hypophyseal stalk is divided and the pituitary gland removed. Postoperative replacement therapy consists of cortisone, 50 mg. a day; thyroid, 120 mg. a day; and nasal insufflation of pitressin powder in those patients manifesting diabetes insipidus. The maintenance of the patient following hypophysectomy has not been difficult. The operative morbidity and mortality are comparable to those of bilateral adrenalectomy.

Attempts have been made to produce complete pituitary suppression by irradiation. In most instances this form of

Fig. 2. M. G. Tumor infiltration of the antrum of the stomach in November 1955. Disappearance of infiltration by October 1956, five months after hypophysectomy.

therapy has failed to eradicate all the pituitary cells, though decrease in pituitary function has been demonstrated. To date, the only successful method of radiation therapy to the pituitary that holds promise of future development is that employed by Lawrence and Tobias with the 324-million-volt machine (16).

The benefits from surgical hypophysectomy have been similar to those following ovariectomy and adrenalectomy. Experience to date is still small. Luft and Olivecrona have performed 55 hypophysectomies for cancer of the breast (17), and report subjective and objective improvement in 22 of 41 cases analyzed. Pearson *et al.* reported 74 cases, with objective regressions in 28 (18). In a review of the literature, Luft noted that of 197 cases evaluated, 110 had remissions (56 per cent). This figure includes patients with apparent stationary disease. Kennedy *et al.* have studied 32 selected patients. Objective regressions occurred in 21 (65 per cent) of these (19). Two additional patients had metabolic remissions.

Hypophysectomy provides another means of altering metabolic status. In patients with intact ovaries or adrenal glands, improvement may be the result in part of suppression of these endocrine glands, comparable to their surgical ablation. A careful selection of patients for hypophysectomy is required. It would appear that a premenopausal patient with advanced cancer of the breast responding to therapeutic castration will, on reactivation of the disease, almost always respond to hypophysectomy. In postmenopausal women responding to estrogenic or androgenic hormone therapy, recurrences will undergo further regression after hypophysectomy. While the number of operations remains small, the role of hypophysectomy in treatment of advanced cancer of the breast is becoming more clearly defined.

Case Report

M. G., a postmenopausal woman aged 54, noticed a mass in the left lateral breast in January 1955. Retraction of the lateral breast was demonstrated by pectoral contraction tests. A diffuse, firm mass was palpable. Multiple axillary nodes were present. There were no supraclavicular nodes. Roentgen examination revealed multiple small osteoblastic metastases in all bones examined. The patient was placed on stilbestrol, 15 mg. daily. Subsequently

there was a complete disappearance of the osteoblastic lesions, so that the roentgenograms were regarded as normal. The primary tumor decreased in size and became softer, and the axillary nodes disappeared.

Improvement was maintained until November 1955, when severe constipation, nausea, and vomiting developed. A large 10 cm. mass was present in the left lower quadrant of the abdomen. Only one finger could be inserted into the rectum because of a hard, constricting perirectal tumor. Roentgen examination revealed dilatation of the stomach and a cone-shaped narrowing of the gastric antrum, apparently due to tumor infiltration of the stomach wall (Fig. 2). In the colon a large mass was demonstrable in the perirectal area, with constriction of the proximal rectum.

The patient was considered too ill for hypophysectomy. Hence, a combination of testosterone propionate, 100 mg. three times a week intramuscularly, and cortisone, 300 mg. a day, was employed. During the subsequent two months there was a marked amelioration of the patient's condition, with cessation of vomiting and improvement in bowel function. However, the masses in the abdomen and rectum did not decrease in size. In January 1955, the cortisone was decreased to 100 mg. daily. Roentgen examination in March 1956 revealed no change in the stomach wall. The palpable masses in the abdomen and rectum had not diminished. The mass in the left breast again became apparent and was diffusely palpable in the outer quadrants.

Because of apparent progression of the cancer, the testosterone and cortisone were omitted and a total hypophysectomy was carried out in May 1956. Following this operation, the patient's weight increased from 175 to 200 pounds, bowel function improved, appetite increased, and the abdominal and perirectal masses disappeared. Five months after the operation some thickening in the rectal area with tenderness could be detected but no discrete mass was felt.

On Oct. 23, 1956, roentgen examination showed the stomach to be nearly normal, with no evidence of tumor infiltration of the wall (Fig. 2). The patient is well one year after operation.

Comment: In this postmenopausal woman objective regression of an advanced breast cancer occurred during estrogen therapy. On reactivation, cortisone and testosterone were employed in an attempt to produce subjective improvement. So successful were the results that hypophysectomy could be carried out though the cancer had continued to progress. A marked regression of this advanced lesion followed hypophysectomy and is at present being maintained.

ANDROGENS

Androgens have been used primarily as palliative agents in advanced mammary cancer with metastases. In the selection of patients for therapy, age is not an important determining factor, since these agents have exerted a favorable effect on the tumor at any stage in life. The major beneficial effects have been on osseous metastases; hence the site of the disease is important in selecting patients for androgen therapy. There is no evidence to indicate that the androgenic hormone should, in any way, be used as a prophylactic agent.

Testosterone propionate has been most commonly employed. The doses have been 150 to 300 mg. weekly in three divided doses, intramuscularly. Symptomatic improvement may appear in two to four weeks, with marked decrease of pain and subjective improvement. There is considerable discrepancy between subjective and objective improvement in response to this compound. Between 55 and 75 per cent of patients with metastatic breast cancer obtain symptomatic benefit. Only 20 to 25 per cent show objective evidence of improvement (21). A still lower incidence of objective regression of soft-tissue metastases has been noted. It would appear that the soft-tissue remissions occur oftener in premenopausal patients, leading to a clinical effect similar to that of castration. The duration of the favorable responses is variable, but recrudescence of signs and symptoms usually appears within one year. To date, it would appear that testosterone propionate is not as effective as castration in the premenopausal group and therefore should not be employed in these patients. After the menopause it is as effective as estrogenic therapy for osseous metastases but does not produce as favorable an effect on the soft-tissue metastases. The use of androgenic hormones, therefore, is limited primarily to postmenopausal women with skeletal involvement.

Administration of large doses of androgenic hormones to the female patient produces disturbing side-effects. The de-

velopment of these changes is more predictable than the desired therapeutic effect. An attempt has been made to develop agents which will be equally effective therapeutically without unfavorable reactions. Compounds with such characteristics deserve investigation, but in order to be of real value they must be as good as or better than testosterone propionate without eliciting changes that are distressing to the patient (3).

Recently a halogenated methyl testosterone has been employed orally in the treatment of advanced breast cancer (20). Objective remissions were obtained in 15 of 29 patients, and definite masculinizing effects were observed. The chief advantage of this new agent is that it is administered orally and is at least as effective as testosterone propionate in producing favorable effects on the breast cancer.

As mentioned above, it has been established that androgenic hormones are to some extent converted to estrogenic hormones (5). The latter metabolic products may be responsible in part for some of the effects noted during androgen therapy. The administration of androgenic hormones has resulted in a stimulation of tumor growth, manifested by the development of hypercalcemia, in 10 per cent of the patients with osseous metastases. This is a serious complication and unless the androgens are withdrawn death may ensue. It is apparent that the role of androgenic agents is less important in the management of breast cancer than has been previously emphasized.

Case Report

E. C., aged 53, had a right radical mastectomy for cancer of the breast in January 1955, with postoperative radiation therapy. In February 1956, she was admitted to the University Hospitals because of gradual onset of anorexia, nausea, vomiting, and back pain. Clinical examination revealed dehydration and weight loss. Extensive osseous metastases were demonstrable roentgenographically, involving multiple bone areas. Metabolic studies were undertaken. There was evidence of severe hypercalcemia and hypercalciuria.

The patient was given 20 mg. of Halotestin (9-alpha-fluoro-11-beta-hydroxy-17-methyl testosterone), orally every day. A decrease in hypercalcemia and hypercalciuria followed, with relief of pain and recalcification of the osseous metastases. This improvement was maintained for five months.

On July 21, 1956, the patient was again admitted to the hospital because of recurrent pain, anorexia, and vomiting. The serum calcium was 12.7 mg. per cent. Stilbestrol, 15 mg. a day, was given from July 21 to Aug. 5. During this time there was an increase in hypercalcemia to 15.1 mg. per cent, accompanied by increasing drowsiness and vomiting. It was apparent that the breast cancer was being stimulated by the therapy.

Because of the previous objective response to hormone therapy it was judged that this patient might respond to hypophysectomy. On Aug. 10, 1956, a total surgical hypophysectomy was performed. Four days later the serum calcium was 9.5 mg. per cent. Subsequently there was an increase in the serum alkaline phosphatase, representing bone regeneration. The patient has shown a marked clinical improvement, with recalcification of the osteolytic metastases

Comment: This postmenopausal patient responded initially to androgenic hormone for a short period of time. Subsequent study revealed that the breast cancer was stimulated by estrogenic hormone. A total surgical hypophysectomy resulted in an abrupt control of the disease process with evidence of objective improvement.

ESTROGENIC HORMONES

The effect of estrogenic hormones on human breast cancer is dependent upon the physiologic status of ovarian activity at the time of their administration. In premenopausal women estrogenic hormones have proved to be accelerators of cancer growth. In postmenopausal women they have been shown to cause regression of metastatic breast cancer. The phenomenon of acceleration in the premenopausal group is supported by the observation that castration in this period produced improvement in up to 50 per cent of patients with breast cancer. For tumors which respond favorably to castration and those which are stimulated by administration of estrogen the term "estrogen-dependent" has been employed by many investigators. It would appear paradoxical that in the premenopausal woman the estrogenic hormone is withheld or removed

and in the postmenopausal woman the same hormone is administered in attempts to control breast cancer. However, a rational understanding of the mechanism involved clarifies this apparent discrepancy.

The *Premenopausal State:* Occurrence of carcinoma of the breast in the pregnant woman is associated with a grave prognosis. It has been suggested that the apparent acceleration of the cancer during pregnancy is due to enhanced vascularity of the breast, and hence, ease of tumor spread, and to increased production of estrogenic hormone or other tumor-stimulating hormones by the ovaries and placenta. Young women with metastatic osseous lesions frequently have increased pain prior to the menstrual period, and metabolic data show increased urinary calcium excretion and occasionally hypercalcemia in this same premenstrual phase. Since there is an increase of estrogenic hormone at this time, it has been suggested that this agent accelerates tumor growth. Furthermore, the administration of estrogenic hormones in *physiologic* doses to young women results in exacerbation or acceleration of the breast cancer.

When, however, *massive* doses of estrogenic hormone (stilbestrol, 1,000 mg. daily) have been administered to women with normal menstrual periods and advanced breast cancer (22), tumor suppression has occurred, with a regression of metastatic masses. It would appear that this large dose brings about pituitary suppression and a secondary ovarian suppression. Only rarely has intensified growth of breast cancer been observed in premenopausal women receiving such massive dosage. It is thus apparent that in such patients a large dose of estrogenic hormone is not in itself a stimulus to tumor growth. Other factors which have been suppressed by its action are apparently more important in stimulating or maintaining cancer growth than is the hormone alone. These observations would suggest that the estrogenic hormone has a dual mechanism in its effect on breast cancer. In small doses in the premenopausal woman it stimulates tumor growth. With massive doses, suppression of other factors or a direct effect on the tumor occurs, with consequent tumor suppression. Practically, however, the administration of estrogenic hormones in the premenopausal age is contraindicated.

The *Postmenopausal State:* Estrogenic hormone administration is indicated primarily for advanced breast cancer in postmenopausal women, regardless of chronological age. Best results, however, are obtained in elderly women. Some 50 per cent of patients with soft-tissue lesions and 20 per cent with osseous lesions are objectively improved by such therapy (21). Estrogenic hormones have provided the longest remissions of any form of hormonal therapy in this age group. Continuous estrogenic hormone administration would appear to be preferable to interrupted or intermittent courses.

The mechanism of action of the estrogenic hormone in the postmenopausal patient has not been clearly delineated. Previous investigations have suggested that the effect is on the stromal tissue surrounding the cancer cells, with the production of elastic tissue hyperplasia and sclerosis (23). It appears that the regressions are, in part, the result of hormonal stimulation of the naturally occurring process of repair which primarily concerns the adjacent stromal tissues. A further possibility is suppression of pituitary function. It may be that estrogenic hormones are capable of suppressing the pituitary gland in postmenopausal women more effectively than in women of premenopausal age.

To date the estrogenic hormones are the most effective single hormonal agent in the management of breast cancer in the postmenopausal age group.

ESTROGENIC HORMONES AND RADIATION THERAPY

Possible relationships between estrogenic and radiation therapy have been suggested. Evidence has indicated that estrogens may increase the radiosensitivity of breast cancer (24), though confirmation of this

has been difficult. Partial regression of lesions after initial treatment with estrogens may permit even more effective radiation therapy, through the use of smaller portals.

Estrogen therapy of recurrent tumor within an area of previous and initially effective radiation is ordinarily not as efficacious as for similar untreated lesions (24). The radiation fibrosis would appear to reduce the vascular supply of the tumor and interfere with the effect of the estrogens. The rate of improvement from estrogen therapy is reduced 50 per cent in areas previously irradiated.

It would therefore seem preferable to employ estrogens first and, when these are no longer effective, to use radiation.

The pathological changes of the tumor bed following regression of the lesion with estrogen therapy are similar to those occurring after irradiation, namely, fibrosis, collagen formation, and a decreased vascular supply. Radiation therapy to areas of reactivation in such sites must be applied with the same caution as if they had been previously irradiated. Failure in this respect may result in necrosis similar to that noted in sites where excessive irradiation is applied.

ADRENAL CORTICOIDS

Use of pituitary adrenocorticotropic hormone is contraindicated in breast cancer because of the direct stimulation of the adrenals, with production of estrogenic and androgenic hormones. These latter agents in themselves may stimulate breast cancer.

Cortisone or Prednisone have been employed in attempts to bring about tumor regression in cancer of the breast. It has been postulated that suppression of the adrenal glands and/or the pituitary gland might bring about improvements similar to those observed following surgical ablation of these glands.

Because of the anti-inflammatory effect of the adrenal corticoids, certain changes may occur during their administration that do not represent specific tumor suppression, but do result in a decrease in size of the mass and an increase in subjective well-being. Peri-tumor infiltration and edema are reduced by these agents. Because of this and the beneficial subjective effects of these agents, palliative benefit may be obtained without specific suppression of the breast cancer.

For specific tumor suppression, an initial dose of 300 mg. daily of oral cortisone or 200 mg. daily of Prednisone should be employed. Once tumor regression occurs, a smaller but persistent maintenance dosage should be maintained. In some instances, however, larger doses are necessary.

In view of the preceding considerations, the patients with breast cancer that would most likely improve with corticoid therapy are those who would be candidates for adrenalectomy or hypophysectomy. The experience of most investigators would verify this assumption. To date, the number of improvements noted with cortisone have not been as great as those with ablative procedures, nor has the duration of improvement been maintained as long as with other forms of therapy. Hence, it would appear that corticoid therapy is to be used as an alternative or secondary choice to hypophysectomy or adrenalectomy.

Massive doses of cortisone have been administered to 34 patients with metastatic breast cancer. Of these, 10 showed objective regression, but in only 3 was this of the quality noted with other forms of hormone therapy. The maintenance of tumor control has continued up to one year in such patients, but not beyond this point.

The corticoids are indicated specifically in patients with severe hypercalcemia that is not controlled by other therapeutic measures, with neurological symptoms of cerebral metastases, with convulsions due to cerebral metastases, with dyspnea due to lymphatic spread of pulmonary metastases, and with jaundice as a result of hepatic metastases. It is obvious that with corticoid therapy one is dealing with far advanced disease. Though specific tumor re-

gression does occur, it is not comparable to that following other forms of hormone therapy. In the terminal patient, in whom no further form of therapy is applicable, the discreet use of corticoids results in the maintenance of well-being and prevention of premature debilitation.

SUMMARY

Management of advanced breast cancer has become an increasingly complex undertaking because of the multiple agents available for the control of this disease. It is apparent that to obtain maximum benefit and maximum survival of the patient, consideration of hormonal therapy should commence at the time that the patient presents herself for initial therapy, including radical mastectomy. It is also advantageous that the case be followed by a physician experienced with all these agents, so that the type of response to the various forms of therapy can be carefully evaluated.

The Premenopausal Woman: There is no doubt that the primary measure for advanced breast cancer in the premenopausal woman is castration. In patients responding to this procedure with regression of metastases, the cancer is hormone-dependent. If no remission occurs it is probable that hormone therapy, of whatever type, will be of little aid in the management of the disease. In those with hormone-dependent tumors no subsequent therapy is needed until exacerbation of the disease occurs. At that time a total surgical hypophysectomy would appear to be the most effective agent. Improvement following this procedure is almost sure to occur. Upon further exacerbation the androgenic hormones may be employed.

It is obvious that various investigators will not agree as to the exact chronological order of the forms of hormone therapy. Where hypophysectomy is not available for tumors recurrent after castration the use of androgenic hormones may be considered. This investigator, however, does not feel that the quality of the response equals that following hypophysectomy. At the present time there appears to be no role for bilateral adrenalectomy, since the improvement following hypophysectomy appears to be more satisfactory and control of the patient is easier.

The Postmenopausal Woman: In the postmenopausal woman with inoperable breast cancer, local recurrence, or metastatic disease, estrogenic hormone administration is the preferred form of therapy. In those patients with only osseous lesions, androgenic hormones are equally effective. Remissions of soft-tissue metastases following estrogen therapy are superior, however, to those obtained with androgens. In cases in which no response occurs to these hormones other forms of therapy are unlikely to succeed. Upon exacerbation of the disease in patients demonstrating improvement following androgenic or estrogenic hormone therapy, a total surgical hypophysectomy will probably result in another remission.

By the judicious use of hormonal therapy, maximum survival of the patient with advanced breast cancer can be obtained.

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REFERENCES

1. SCHINZINGER: Das Karzinom der Mamma. München. med. Wchnschr. **52**: 1724–1725, 1905.

2. BEATSON, G. I.: On the Treatment of Inoperable Cases of Carcinoma of the Mamma. Lancet **2**: 104–107, 162–165, 1896.

3. NATHANSON, I. T., AND KELLEY, R. M.: Hormonal Treatment of Cancer. New England J. Med. **246**: 135–145, Jan. 24; 180–189, Jan. 31, 1952.

4. KENNEDY, B. J.: Extirpative Endocrine Therapy for Advanced Cancer of the Breast. Am. J. Med. **21**: 721–727, November 1956.

5. NATHANSON, I. T., ENGEL, L. L., KENNEDY, B. J., AND KELLEY, R. M.: Screening of Steroids and Allied Compounds in Neoplastic Disease. In Symposium on Steroids in Experimental and Clinical Practice, edited by A. White. Philadelphia, Blakiston Co., 1951, pp. 379–405.

6. DAO, T. L.-Y., AND HUGGINS, C.: Bilateral Adrenalectomy in the Treatment of Cancer of the Breast. Arch. Surg. **71**: 645–657, November 1955.

7. CADE, S.: Adrenalectomy for Breast Cancer. Brit. M. J. **1**: 1–4, Jan. 1, 1955.

8. PEARSON, O. H., LI, M. C., MACLEAN, J. P., LIPSETT, M. B., AND WEST, C. D.: Management of Metastatic Cancer. J.A.M.A. **159**: 1701–1704, Dec. 31, 1955.

9. SITTENFIELD, M. J.: Influence of Anterior Lobe of Pituitary on Growth of Sarcoma and Carcinoma. A. Res. Nerv. & Ment. Dis. Proc. (1936) **17**: 466–470, 1938.

10. MOON, H. D., SIMPSON, M. E., LI, C. H., AND EVANS, H. M.: Neoplasms in Rats Treated with

Pituitary Growth Hormone. I. Pulmonary and Lymphatic Tissues. Cancer Res. **10**: 297–308, May 1950.

11. PEARSON, O. H., RAY, B. S., HARROLD, C. C., WEST, C. D., LI, M. C., MACLEAN, J. P., AND LIPSETT, M. B.: Hypophysectomy in the Treatment of Advanced Cancer. Tr. A. Am. Physicians **68**: 101–111, 1955.

12. JESSIMAN, A.: In Symposium on Hypophysectomy, New York, N. Y., March 19–20, 1956. To be published by Charles C Thomas, Springfield, Ill.

13. NATHANSON, I. T.: In Discussion of Arhelger, S. W., and Huseby, R. A.: Estrogen-Androgen Antagonism: Histological Studies of Mammary Gland and Vaginal Grafts of Male Mice Receiving Estrogens. In Proceedings of First Conference on Steroid Hormones and Mammary Cancer sponsored by the Therapeutic Trials Committee of the Council on Pharmacy and Chemistry of the A.M.A. Chicago, A.M.A., 1949, p. 156.

14. KENNEDY, B. J., PEYTON, W. T., AND FRENCH, L. A.: Total Hypophysectomy in Advanced Breast Cancer. Bull. Univ. Minnesota Hosp. **26**: 528–551, 1955.

15. PEARSON, O. H., RAY, B. S., HARROLD, C. C., WEST, C. D., LI, M. C., MACLEAN, J. P., AND LIPSETT, M. B.: Hypophysectomy in Treatment of Advanced Cancer. J.A.M.A. **161**: 17–21, May 1956.

16. LAWRENCE, J. H., AND TOBIAS, C. A.: Radioactive Isotopes and Nuclear Radiations in the Treatment of Cancer. Cancer Res. **16**: 185–193, March 1956.

17. LUFT, R., OLIVECRONA, H., IKKOS, D., NILSSON, L. B., AND LJUNGGREN, H.: Hypophysectomy in the Treatment of Malignant Tumors. Am. J. Med. **21**: 728–738, November 1956.

18. PEARSON, O. H.: Present Status of Adrenalectomy and Hypophysectomy in Treatment of Advanced Breast Cancer. In Proceedings of the Third National Cancer Conference, Detroit, Mich., June 4–6, 1956. Philadelphia, J. B. Lippincott Co., 1957, pp. 277–285.

19. KENNEDY, B. J., FRENCH, L. A., AND PEYTON, W. T.: Hypophysectomy in Advanced Breast Cancer. New England J. Med. **255**: 1165–1172, Dec. 20, 1956.

20. KENNEDY, B. J.: Fluoxymesterone in the Treatment of Advanced Breast Cancer. To be published in Cancer.

21. NATHANSON, I. T.: Clinical Investigative Experience with Steroid Hormones in Breast Cancer. Cancer **5**: 754–762, July 1952.

22. KENNEDY, B. J.: Effects of Steroids in Women with Breast Cancer. In Hormones and the Aging Process. New York, Academic Press, 1956, pp. 253–272.

23. EMERSON, W. J., KENNEDY, B. J., GRAHAM, J. N., AND NATHANSON, I. T.: Pathology of Primary and Recurrent Carcinoma of Human Breast after Administration of Steroid Hormones. Cancer **6**: 641–670, July 1953.

24. NATHANSON, I. T.: Sex Hormones and Castration in Advanced Breast Cancer. Radiology **56**: 535–552, April 1951.

SUMMARIO IN INTERLINGUA

Le Stato Presente del Therapia Hormonal in Avantiate Cancere Mammari

Le selection del therapia pro avantiate cancere mammari es determinate per le objectivo de supprimer le factores que sustene o accelera le crescentia del tumor e de administrar agentes hormonal que es antagonistic al crescentia del tumor. Le sequente mesuras es considerate: (1) Suppression del ovarios; (2) suppression del glandulas adrenal; (3) suppression del glandula pituitari; (4) administration de hormon androgene; (5) administration de hormon estrogene; e (6) administration de hormon adrenocortical.

Le Femina Ante le Menopause.—Le mesura primari in le tractamento de cancere avantiate del mammas ante le menopause es castration. Disparition de metastases in responsa a iste mesura indica que le tumor depende de hormones. In tal casos nulle therapia subsequente es necessari usque un recurrentia es apparente. Alora, total hypophysectomia chirurgic es le mesura de election e resulta in melioration con alte grados de certitude. In caso de exacerbation ulterior, hormones androgene pote esser empleate. Tumores que non responde favorabilemente al castration initial es generalmente non influentiabile per non importa qual typo de therapia hormonal.

Le Femina Post le Menopause.—Therapia a hormon estrogene es le tractamento de preferentia pro non-operabile cancere mammari, pro recurrentias local, e pro lesiones metastatic al periodo postmenopausal. Hormones androgene es equalmente efficace si le affection es restringite a metastases ossee. Metastases in histos molle responde minus ben al androgenos. In patientes qui manifesta melioration gratias a iste hormones sexual, le remission de subsequente recurrentias es probabilemente effectuabile per medio de hypophysectomia.

Per le uso judiciose de therapia hormonal, le superviventia maximal del patiente con avantiate cancere mammari pote esser obtenite.

The Role of the Surgeon in Advanced Cancer[1]

GRANTLEY WALDER TAYLOR, M.D.

THE MANAGEMENT of the advanced cancer patient is very likely to be best handled as a joint enterprise. My own experience is of intimate, close association with my colleagues in the radiological department and in the department of medicine. We *all* are working toward a common goal.

One of the basic requirements of any such régime of co-operative enterprise is that some one individual guide the show, or at least be accessible to the patient to explain what is happening, and to maintain his morale and that of his family during such a program. Very often it falls to the surgeon to assume this role of the patient's Physician (with a capital P) because so often the advanced case represents the end-result of the surgeon's failure at some earlier time. The basis of *rapport* with the patient and his family has already been established, and they turn automatically to the one whom they have come to know for guidance during the later stages of this problem. He cannot slough off onto the radiologist or the medical consultant the responsibility for management, interpretation, explanation, etc.

Basically, the surgeon must frequently be the Physician and maintain an attitude of hopefulness and encouragement to see the cancer patient through the final and disheartening phases of his illness. There are other things, specifically surgical, which are up to the surgeon. First of all, in advanced and incurable cancer the question is—Is it really advanced and incurable? In the last few years we have seen a tremendous emancipation of surgery from some of the limitations formerly obtained in this field. With recent advances in surgical technic, in anesthesia, and in the use of transfusions, the surgeon can do almost anything to a patient.

Cancer is potentially curable surgically, by ablation or eradication, as long as it remains a localized process. We now have the concept of the ultra-radical surgical approach which Dr. Brunschwig so well employs and exemplifies at the Memorial Hospital in New York.

The criterion becomes not whether one *can* perform an apparent miracle of ultra-radical surgery *and* get away with it, but whether he is doing something which is worthwhile to the patient. I think that the problem is not so much prolonging life merely to prove that life *can* be prolonged, or eradicating disease merely to prove that surgeons today can eradicate almost anything, but eradication of the disease to give the patient a tenure of useful, comfortable, and enjoyable existence. That *must* be the measure of the worthwhileness of the surgery we propose to employ.

Dr. Brunschwig, I am sure, will maintain that a woman can be a perfectly successful, let us say, stenographer, though her pelvic organs have been completely eradicated. Many younger women may feel that these are essential to their occupational success but it is certain that they can still ply their trade without them. But, seriously, one *must* evaluate the individual in whom he is carrying out these procedures before he says that they are worthwhile.

We can do ultra-radical operations and eradicate cancer as long as it is a localized process. We must decide whether we are justified in doing it on the basis of the patient's morale, social status, responsibilities, and capacity for adjusting to the disfigurement or the mutilation or limitations of function which we impose by our procedures.

Another role of the surgeon lies in the attack on the solitary or localized metastatic process. We are all familiar with the

[1] Presented as part of a Symposium and Panel Discussion on Management of the Patient with Advanced Cancer, at the Forty-second Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 2–7, 1956.

rare performance of a partial pneumonectomy for what appears to be an isolated pulmonary metastasis. The same situation exists in neurosurgery. Ever so often our neurosurgical colleagues will have operated upon a brain tumor to find it is a metastasis and that the patient has enjoyed a long period of freedom from disease, even though the lesion was metastatic—presumably disseminated from some undiscovered or only lately discovered focus. The same applies, though more rarely, to isolated bone metastases.

It is reasonable to consider the prospect of radical surgical extirpation of these secondary lesions even though they may be remote blood-borne metastases, provided they are unique or localized or encompassable in a series of procedures.

We have a number of joint enterprises for the management of advanced cancer, and that is where Dr. Schulz, Dr. Robbins, and I get along very well together. They handle what they can and then we do what we need to do surgically, or *vice versa*. It seems to me we spend a good deal of time taking in each other's washing but it is always good and it is deliberately planned.

A familiar example is the method which Dr. McWhirter has so widely publicized—the joint handling of breast cancer by the surgeon and radiologist. I don't go along with McWhirter one iota but it is an example. Some head and neck cancers are very well handled—so far as the local disease is concerned—by intensive irradiation, and then perhaps can be benefited by a properly planned neck dissection or some further operative procedure.

Then there is the role of the surgeon in the reconstruction following cure by some other means—the plastic operations which are carried out, the reconstruction of jaws and other procedures which may be carried out long after the disease has been eradicated.

I was not supposed, however, to talk about curing advanced cancer; I was supposed to talk about palliation. I think we must thank Dr. Schulz[2] for his sermon and especially for the point which he brought out; that is, that palliation consists not simply in treating the disease for the sake of treating the disease but treating the disease with the hope of relieving the patient's symptoms.

Dr. Kennedy[3] mentioned one field in which the surgeon can be helpful, i.e., certain procedures for altering the hormonal environment. He spoke particularly of castration. He and I put our heads together beforehand and decided that adrenalectomy is simply an evolutionary phase in development and that it is going to be abandoned as a procedure because there are so many things that are bad about it. Hypophysectomy is simpler and more effective.

We can also do palliative surgery for relief of the patient's symptoms in the form of débridement. We don't let a patient with arteriosclerotic gangrene of the leg lie in bed with a necrotic, gangrenous leg. We amputate. We don't expect thereby to modify the course of his arteriosclerotic disease but we do make him a more comfortable person to have around the house. People can care for him without holding their noses and he can get along much more happily than with a gangrenous extremity.

I think the same thing applies to the advanced mammary cancer which is fungating, ulcerating, bleeding, discharging, and causing a putrid odor. Frequently we can eradicate these gangrenous areas due to cancer as a purely palliative procedure, a débridement of the sort which we carried out on so many war wounds.

Then, of course, there are the measures which Dr. Schmitz touched upon—relief of obstruction by by-passing operations, tracheotomies, gastrostomies, colostomies, ureterostomies, etc. Again I think the measure of the utility of these procedures should be based on whether they actually contribute to the patient's comfortable existence; that their object should be not solely to prolong life but to relieve discomfort and contribute, if we can, to ease of

[2] See page 321.

[3] See page 330.

management and possible enjoyment of life.

Finally, we come to the surgical measures for control of pain. We can handle fractured extremities with the Küntschner rod or with an extension of the rod which will do a great deal to relieve the pain of the patient with metastatic breast cancer. We can carry out various neurosurgical procedures, either peripheral blocks with a needle or excision of nerves or subarachnoid blocks or cordotomies or prefrontal lobotomies.

This is merely a brief recapitulation of some of the things which the surgeon can do or may be able to contribute to the care of the patient with advanced cancer.

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SUMMARIO IN INTERLINGUA

Le Rolo del Chirurgo in Cancere Avantiate

In le forma de un breve recapitulation, le autor lista certes del contributiones que le chirurgo pote facer in le manipulation de patientes con cancere avantiate.

Le tractamento de cancere avantiate es un interprisa cooperative in que le chirurgo debe frequentemente prender le rolo de medico-in-chef, accompaniante le patiente a transverso le discoragiante phases final de su morbo. Inter le responsabilitates specificamente chirurgic, le prime es decider si le condition es vermente avantiate e incurabile. Alteres es attaccar solitari o localisate processos metastatic, cooperar con le radiologo in le spero de effectuar un curation, e effectuar mesuras de chirurgia reconstructive post le eradication del morbo per altere medios.

Quanto al mesuras de valor purmente palliative, mention es facite del alteration del ambito hormonal (per castration, hypophysectomia, etc.), de debridement pro alleviar le symptomas, de alleviation de obstructiones per varie manovras de shuntage, e de varie mesuras chirurgic pro alleviar le dolor.

DISCUSSION ON MANAGEMENT OF THE PATIENT WITH ADVANCED CANCER

(Papers by Schulz; Schmitz and Isaacs; Kennedy; Taylor)

Howard B. Hunt, M.D., Moderator: It seems particularly appropriate that a symposium on advanced cancer should be presented as part of the scientific program of the Radiological Society of North America. Sooner or later the majority of patients with cancer reach the radiologist, who should serve not only as radiotherapist but also as a consultant in the whole field of cancer therapy. It is essential, therefore, that he be familiar with and able to evaluate not only the possible contributions of radiotherapy in the management of a particular lesion of an individual patient, but also the potential roles of surgery, endocrine therapy, chemotherapy, and proper clinical management.

Inasmuch as optimal therapy for the patient with advanced cancer involves the skills of the internist, the general surgeon, the regional specialist, and the radiotherapist we have included in our panel representatives of these several fields in cancer therapy: Dr. Grantley W. Taylor, Surgeon and Director of the Cancer Clinic, Massachusetts General Hospital, Boston; Dr. Milford D. Schulz, Radiologist and Director of Radiotherapy, Massachusetts General Hospital, Boston; Dr. Herbert E. Schmitz, Gynecologist, Stritch College of Medicine, Chicago; Dr. B. J. Kennedy, Endocrinologist and Chemotherapist, University of Minnesota, Minneapolis.

The first case presented by Dr. Kennedy in his formal paper was that of a premenopausal woman of forty-two years with pelvic metastases from cancer of the breast. It is agreed that castration is a desirable approach in the management of this patient. The first question is: Should castration be done by oophorectomy or by pelvic irradiation. We shall put this question to Dr. Schulz. Dr. Schulz, is it practical to inactivate ovarian function by radiotherapy and gain an effective clinical response such as occurred in Dr. Kennedy's case following oophorectomy?

Dr. Schulz: There is no question, I am sure, that you can produce apparent cessation of ovarian function effectively in premenopausal women by radiotherapy, but I do not know how far radiotherapy goes in causing *absolute* cessation of ovarian function. I would like to hear Dr. Taylor discuss this subject.

Dr. Taylor: Dr. Hunt, Dr. Schulz, Dr. Rob-

bins, and I have discussed this problem at length among ourselves, and I think there is no question but that oophorectomy gives complete, thorough, and immediate eradication of ovarian function. The question is whether we actually must have complete, thorough, and immediate eradication of ovarian function in these cases. Certainly patients who have had an artificial menopause induced by x-irradiation have in many cases shown regressions just as striking as reported by Dr. Kennedy following surgical castration, and certainly we feel that, if there is any contraindication to subjecting the patient to even this relatively minor operative procedure, we can go ahead with x-irradiation for production of the menopause. Actually, the response to irradiation is a little more leisurely in manifesting itself, but my feeling is that in many cases it has been just as effective. Perhaps Dr. Kennedy may have some further information on this subject.

Dr. Kennedy: I think, if one reviews the literature, he might gain the impression that surgical castration is preferable. The difficulty is that in most papers dealing with the irradiation menopause the dose cited is one which produces amenorrhea rather than a dose that would be truly castrative in nature. This precludes a fair comparison. I think it would be appropriate to ask Dr. Schulz what he considers a true castrating dose.

Dr. Schulz: The dose varies somewhat with the age of the patient. For a young woman I think more radiation is required than in an older one. To a patient in the forties we give 1,500 r to the ovaries in a week. Below that age I suspect it takes a little more.

Dr. Hunt: The relative completeness of suppression of ovarian function can be most readily determined from the vaginal smear, in our experience.

Dr. Schulz, here is another question. Might you gain relief from pelvic pain more quickly if the lesion were irradiated locally along with ovarian inactivation?

Dr. Schulz: Yes, probably so. Symptomatic improvement following castration is delayed; more immediate relief may be obtained by a dose in the order of 1,500 to 2,000 r directly into the area of bony metastases.

Dr. Hunt: Dr. Kennedy, do you see any disadvantage in utilizing such combined therapy?

Dr. Kennedy: It might have one disadvantage, in that, if castration and local irradiation are performed together, one can't be sure what the effect of castration has been, and I think it is important to know whether the cancer is endocrine-dependent. We should learn whether the patient responds to castration as a primary procedure. Knowing that she responded well to castration, I would be able, when reactivation of her disease occurs, to look her in the face and say, "You need a hypophysectomy," without feeling that I may be doing an injustice. Her chances of getting a further remission are exceedingly good.

Dr. Hunt: Thank you, Dr. Kennedy, A question has come from the audience relating to hypophysectomy and will be put to Dr. Taylor and Dr. Kennedy. "How do hypophysectomy and adrenalectomy compare as to morbidity and mortality? How does the postoperative management of these cases compare?"

Dr. Taylor: Dr. Kennedy has just worked this material up and reported it in some detail and I think he can speak with greater authority than I. I'm scared to death in taking care of a postoperative adrenalectomy patient.

Dr. Kennedy: I think the patient who has had an adrenalectomy has a longer hospital course than the patient undergoing hypophysectomy. Removal of the adrenals creates an abrupt and total deficiency which makes the electrolyte balance at least very labile. The patient who has a hypophysectomy is usually eating the next day, is ambulatory within a week, and can be discharged within two weeks. The ease in management is much greater than with adrenalectomy. It takes 50 mg. of cortisone, 120 gm. of thyroid, and occasionally pitressin, but we can feel secure even when such a patient is several hundred miles away, knowing that the family physician is capable of managing the case without requiring a lot of chemical data daily or weekly. On the other hand, the adrenalectomized patient, being so labile, can drop dead merely from getting too hot, or may have trouble for any number of reasons. I think, therefore, that the morbidity from hypophysectomy is much less than with adrenalectomy.

As far as the mortality is concerned, the series of hypophysectomies in the whole nation is still small, but we have not had a death for almost two years. I think that, with selection of patients both for time and physical status, either procedure should have a relatively low mortality.

Dr. Hunt: Thank you very much, Dr. Kennedy. This is a fascinating subject, but we must move on to other problems. Dr. Schulz, will you please comment regarding your experience with the reirradiation of carcinoma of the cervix in the light of the presentation by Dr. Schmitz.

Dr. Schulz: I am certainly encouraged to see the remarkable salvage by radiotherapy which Dr. Schmitz has obtained following failure of prior radiation therapy. Our experience has been

such as to make me afraid of trying to re-irradiate in such cases. I think that, if a patient has had adequate radiotherapy for carcinoma of the cervix and this has failed, she has about lost her chance for cure as far as irradiation is concerned. Palliation? Yes. But even this must be entered upon with caution. I think the same thing can be said for radiotherapy following failure by surgery. There are few cases in which you can really rescue the patient and give a long-term survival.

Dr. Hunt: Dr. Murphy presented some equally encouraging statistics here last year on the re-irradiation of cervical cancer. It would seem that control of recurrences might well be possible when the recurrence is in an area wherein the dosage was well under the tolerance limit, permitting the second radiotherapy to be effective and tolerable. Certainly we must re-evaluate this so-called initial treatment which, on review, may be found significantly low in the area of persistent or recurrent disease. We have found postoperative residual or recurrent carcinoma of the cervix uteri to be most effectively handled by interstitial radium implantation and in some cases by transvaginal roentgen therapy.

Dr. Schulz, would you please present the next case history.

Dr. Schulz: A 32-year old man was referred to us for radiotherapy because of multiple bony metastases. A year prior to admission a mediastinal tumor had been incompletely removed and treated by radiotherapy of unknown dosage. Histologic material showed a tumor which resembled seminoma of the testis, but careful examination of the testes showed no tumor. Radiographic studies showed metastases in the hips, pelvis, and cervical spine. When we saw the patient, he was scarcely able to walk; he used two canes and was in great pain. Because of the widespread nature of his disease, it was felt that palliation was about all that we could offer him. Consequently he received only 1,500 r in three or four days, into each of the painful areas. In each instance the pain was promply relieved and now, curiously enough, he has had no recurrence of pain at any place, and radiographs of the pelvis show persistent healing of these multiple bony metastases.

I present this case to show that multiple bony metastases of a radiosensitive tumor, even when treated with minimum radiation, are sometimes controlled for long periods of time. I don't doubt but that this fellow is going to get into trouble some day again, but I know pretty much what we can do for him in the relief of pain.

Dr. Hunt: Dr. Kennedy, would you like to comment about the use of some of the chemotherapeutic agents in the management of testicular tumors?

Dr. Kennedy: There is a group of compounds which have produced regression of some seminomas. These compounds are quite toxic and cause severe neuritis. I would certainly think that such compounds ought to be confined to the patient who has gone through the period of radiation therapy and used only when the radiation therapist feels that he can no longer do any good. Their results certainly do not excel the known improvement that follows radiation therapy of seminoma.

Dr. Hunt: I would like to ask Dr. Schmitz how he feels about the treatment of metastatic dysgerminoma of the ovaries, a lesion of comparable radiosensitivity with seminoma in the male.

Dr. Schmitz: I feel the same about all ovarian cancers, that is, that they should be irradiated either preoperatively or postoperatively. I have shown that, in our series at least, there are some apparent benefits from irradiation and we frequently see situations in which the tumor responds and the patient becomes operable. Certainly, if the mass shrinks and becomes movable, surgical removal is then the better treatment for the patient with ovarian disease.

Dr. Hunt: Thank you, Dr. Schmitz. I had hoped to bring out that dysgerminomas of the ovary were in general fully as radiosensitive and subject to control by radiation as seminomas of the testicle. I shall ask Dr. Taylor to present the next case.

Dr. Taylor: This is a case I can recapitulate rapidly. The patient was an obese woman, not what you would call a prime operative risk. She had an extensive carcinoma involving the tongue, which one of my radiologist colleagues undertook to treat (with my blessing). The margins of the lesion were poorly defined; it was probably over an inch in greatest diameter, with extension to the floor of the mouth. There was no obvious metastatic disease in the neck. The biopsy report was epidermoid carcinoma, Grade III. X-ray therapy was given between May 18 and June 25, 1946; for a total of 4,500 r through a right lateral port and 3,900 r through a submental port.

In September an enlarged lymph node was noted in the upper neck, along with some residual induration in the tongue. In October 1946, a right radical neck dissection was carried out. Five 10-mg. platinum radium needles were implanted in the tongue for a total of 2,100 milligram hours. Pathologic examination confirmed the presence of metastases in one lymph node. Following the radium implantation and node resection, a sloughing painful ulcer developed on the tongue and gum, with extensive bone necrosis evident on x-ray examination. Enlarged lymph nodes developed in the left side of the neck. Accordingly, in April 1947, a modified left radical

neck dissection was performed, with confirmation of metastases. In July, 1947, a transoral sequestrectomy was carried out, following which the mouth healed.

The patient has been seen at intervals since the last operation, nine years ago, and has remained well. There is some distortion of the tongue, with limitation of function, but no significant impairment of speech or deglutition.

Here we have a patient treated by implantation of radium in the tongue, a bilateral radical neck dissection for positive nodes, and a subsequent sequestrectomy of the mandible, illustrating the joint enterprise of radiologist and surgeon. Neither of us, I think, would have effectively controlled the situation. She is a well woman. She can do everything but eat corn on the cob and enjoys perfect health, with continued gratitude to the radiologist and to the surgeon who took care of her.

Cystic Angiomatosis of Bone[1]

RAYMOND GRAMIAK, M.D.,[2] GILBERTO RUIZ, M.D.,[3] and FRANK L. CAMPETI, M.D.[4]

THE CLASSICAL descriptions of Bucy and Capp (3) established the presently accepted roentgen criteria for the diagnosis of cavernous hemangioma of bone. In recent years, a rare and somewhat atypical form of cavernous hemangioma, aptly labeled "cystic angiomatosis" by Jacobs and Kimmelstiel (8), has been reported. As the name implies, there is widespread distribution of purely cystic lesions, which show none of the usual x-ray findings associated with hemangioma of vertebrae or flat bones. Nor are the lesions in the long bones entirely typical. A case of cystic angiomatosis, correctly diagnosed prior to definitive biopsy, will be presented in this article. So far as we know, it is the first to appear in the radiologic literature.

A 15-year-old Negro boy was admitted to the Rochester Municipal Hospital on Oct. 28, 1955, with a fracture of the left femur sustained while playing football. Emergency roentgenography showed that the fracture had occurred in a cystic area and that several other cysts were present in the femoral shaft. There had been a fracture of the right humerus in 1950 and a review of the roentgenograms obtained at that time showed that this too had occurred in a cystic lesion, and that cysts were present in the humerus and scapula. The family history was non-contributory.

Fig. 1. Postero-anterior and lateral roentgenograms of skull and cervical vertebrae. The widespread and extensive cystic angiomas are striking. Of especial interest is the large lesion, which occupies much of the body of C-2 and extends into the base of the odontoid process. There is no suggestion of vertical striation of the involved vertebra.

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Fig. 2. Anteroposterior roentgenogram of thoracic and lumbar vertebrae. Many of the ribs contain cystic angiomas, particularly the left fourth rib. The right pedicles of T-8 and L-2 are also cystic. Attention is especially directed to the regeneration of normal bone in the resected left ninth rib.

Physical examination demonstrated, in addition to the fracture, a harsh Grade I systolic murmur. On palpation no masses were found to be in the abdomen.

Blood studies showed: hemoglobin, 14.4 gm. per cent; hematocrit, 42; corrected sedimentation rate, 13 mm. in an hour; white cells, 5,800; calcium, 9.4 mg. per cent; phosphorus, 5.5 mg. per cent; acid phosphatase, 1.9 Bodansky units; alkaline phosphatase, 12.5 Bodansky units; total protein, 7.4 gm. per cent, with an A/G ratio of 4.5/2.9; cholesterol, 145 mg. per cent. Analyses of the urine and feces were negative.

A roentgen survey of the skeleton demonstrated widespread involvement of many bones by benign-appearing cystic lesions (Figs. 1–5). When the films were first seen, the possibility of reticuloendotheliosis was suggested.

Exposure of the skull for biopsy revealed a circular area darker than the surrounding normal bone. A small hole was bored through the outer table. At this point, brisk bleeding originating between the tables of the skull, was encountered. A circular area about 1 cm. in diameter was removed with a scalpel and an empty cavity was entered. Bleeding was controlled with suction and bone wax. On pathological study the material obtained at biopsy was reported as normal bone.

Five months later, the patient was seen with a spontaneous hemarthrosis of the knee, which responded to general supportive measures and aspiration of blood from the joint. Roentgenograms showed no local bony defects. It was at this point that the diagnosis of cystic hemangiomatosis was suggested, based on the x-ray appearance of the lesions and their tendency to bleed.

Right Left

Fig. 3. Anteroposterior roentgenograms of left and right humeri. The shortening and widening of the right humerus are probably the result of an old fracture. A "cyst" can still be seen in the fracture area. The lesion in the humeral metaphysis near the epiphyseal line is "new" and was not present six and a half years earlier. The scapular angioma remained unchanged during this interval.

On April 28, 1956, the left ninth rib was partially resected for pathologic study. Grossly, a cystic area measuring 6 mm. in diameter was found thinning the cortex on one side to a delicate shell and extending through the rib to the opposite cortex (Fig. 6). The bone throughout the remainder of the specimen was dense, and no normal marrow cavity was apparent. Microscopically the bony trabeculae appeared thickened but they were architecturally normal. The hematopoietic tissue was normal. The walls of the large cystic spaces contained delicate connective tissue lined with flat endothelial cells. Pink-staining coagulum was present in most of the cystic spaces (Fig. 7). Within the connective tissue were thin-walled vascular spaces,

some of which contained red blood cells; similar spaces lined with endothelium were encountered in the marrow. The pathologic diagnosis was angiomas of the rib.

Cinefluorographic studies were made of the left humerus. No pulsation of the large cystic lesion was demonstrated.

Lesions in the left humerus and second cervical vertebral body were selected as potentially the most dangerous from the standpoint of fracture, and were treated by irradiation, each receiving 2,000 r at 250 kv over a period of fourteen days. Roentgenograms at the completion of therapy demonstrated no change in the appearance. The follow-up has been too short, however, for determination of the full response to irradiation.

There was no evidence of extraskeletal involvement except for the possibility of a relationship to the spontaneous hemarthrosis.

Fig. 4. Anteroposterior roentgenogram of the pelvis. The left ilium contained the largest "cyst." It measured 6.0 cm. on the original films. Wide variation in size of lesions is demonstrated.

DISCUSSION

Incidence: Hemangiomas of vertebral bodies are frequent autopsy findings. Töpfer, in 1928, found the incidence to be 11.9 per cent in 2,154 autopsies (16). Extravertebral benign angiomas are considerably less common; Jacobs and Kimmelstiel (8), in 1953, stated that only 41 cases had been reported. They found 17 cases of multiple benign angiomas involving the skull and extremities, but none with the cystic appearance and widespread distribution of the two they presented. Ritchie and Zeier (11) have since added a case and have called attention to another reported by Parsons and Ebbs (10), making a total of 4 known examples of cystic angiomatosis. Shennan (12) was very likely dealing with the same entity. His patient had extensive cystic angiomas in the viscera and a lesser number in the sternum, clavicles, and vertebral bodies; the femoral marrow also showed angioma his-

TABLE I: DISTRIBUTION OF BONY LESIONS

Case	Skull	Vertebrae	Pelvis	Clavicle	Scapula	Ribs	Humerus	Radius	Ulna	Metacarpals	Femur	Tibia	Fibula	Inconclusive Biopsy	Definitive Biopsy
Jacobs and Kimmelstiel	X	..	X	..	X	X	X	..	..	..	X	..	..	Pelvis	Rib
Jacobs and Kimmelstiel No. 2	X	..	X	..	X	X	X	X	X	..	X	X	..	None	Rib
Parsons and Ebbs*	X	..	X	..	..	X	X	..	..	..	X	X	X	Sternum	Autopsy
Ritchie and Zeier†	X	..	X	X	X	X	..	..	..	..	X	X	..	Tibia	Rib
Gramiak *et al.*	X	X	X	..	X	X	X	..	X	X	X	X	..	Skull	Rib

* Involvement also of liver, spleen, retroperitoneal tissues, lung, thymus, pericardium.
† Involvement also of spleen.

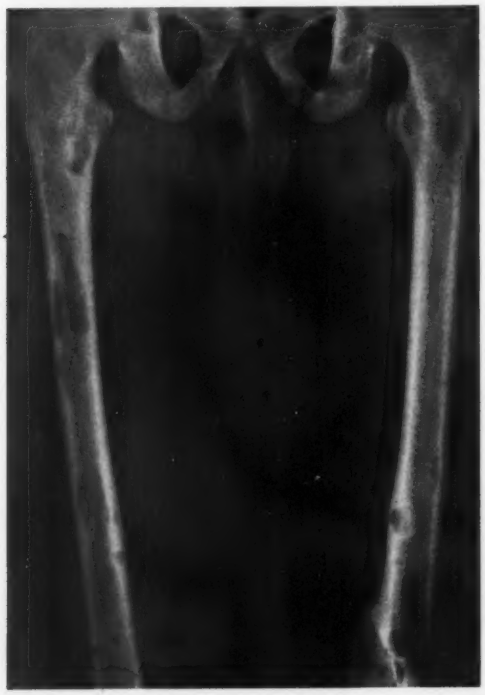


Fig. 5. Anteroposterior roentgenograms of both femora. There is good healing of the fracture of the left femur. Some of the cysts are purely cortical, others occupy a medullary position.

tologically. Since the bone lesions were not studied roentgenologically, however, this example is not being considered in the present discussion.

Distribution of Lesions: The skull, pelvis, ribs, and femora have been affected in all known instances of this condition (Table I). In 4 of the 5 cases (including our own), the humerus, tibia, and scapula contained lesions. Less frequently, cystic changes were demonstrated in the fibula, radius, ulna, vertebrae, metacarpals, sternum, and clavicles. Other organs also may contain cystic angiomas, and these, in fact, may be the major cause of symptoms; the spleen is the most frequent site, but the lungs, thymus gland, liver, retroperitoneal region, and pericardium have been involved.

Diagnosis: The diagnosis is difficult to establish clinically, even though the bone changes are evident. Presenting symptoms may be related to swelling about a bone lesion or a pathologic fracture through a cyst, or they may be secondary to cystic angiomas involving the viscera, with ab-

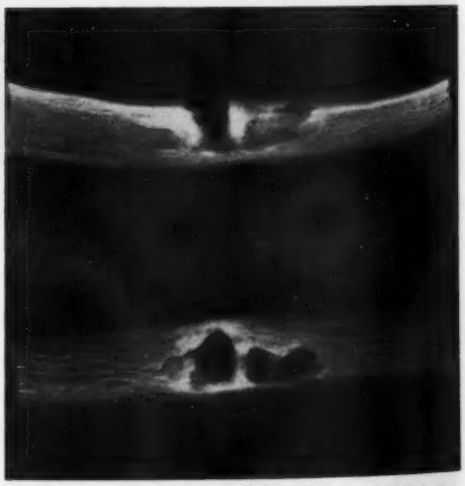
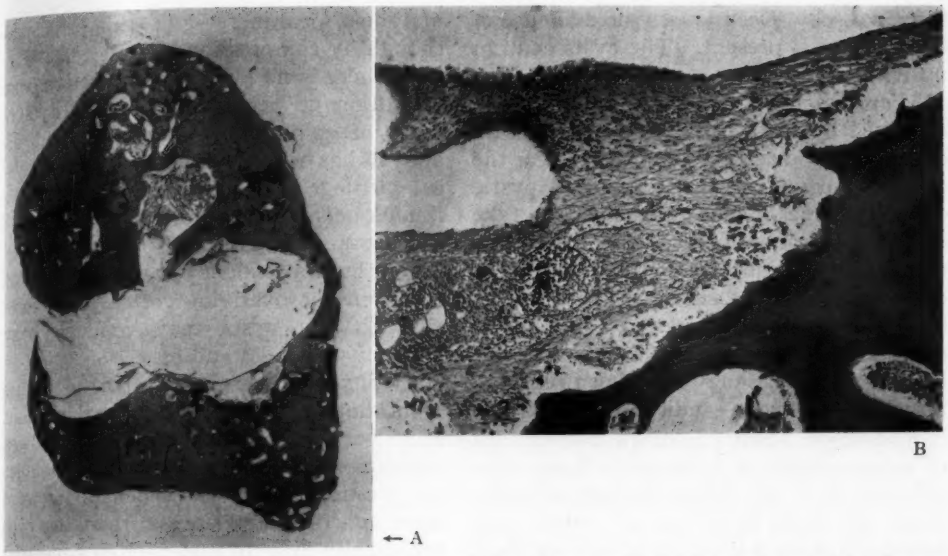


Fig. 6. Anteroposterior and lateral roentgenograms of resected rib. Note the empty appearance of the lesion, with no suggestion of trabeculation or fibrillation. Some inward bulging of the rib is present. The local increase in bony density is not a frequent finding in other areas.



← A B

Fig. 7. A. Low-power photomicrograph of the resected rib. The "empty" cystic spaces in cortical bone are demonstrated.
B. Photomicrograph of cyst wall (×100) showing the lining of endothelial cells. There are smaller endothelial-lined spaces packed with red blood cells within the surrounding connective tissue.

dominal pain, bloody ascites, cough, or hemoptysis.

The blood chemistry is invariably normal. The presence of an enlarged spleen and cystic bone lesions has led to the preoperative diagnosis of reticulo-endotheliosis. Parsons and Ebbs (10) have provided an excellent discussion of generalized angiomatosis, and have pointed out the similarities between this condition and reticuloendotheliosis. Definitive diagnosis of cystic angioma is established by biopsy, excision of a portion of an affected rib being the procedure of choice. Attempts to obtain biopsy material from any other bone have uniformly led to inconclusive results, mainly because of bleeding and difficulty in removing adequate tissue for diagnosis.

Pathology. Two varieties of benign angioma are generally recognized: capillary and cavernous. Hemangiomas occurring in bone are almost exclusively cavernous; the capillary type is exceedingly rare (13). Ewing (4) differentiated between two forms of cavernous hemangioma on the basis of behavior. One is an essentially static form with only local manifestations of its presence. The other, though apparently benign microscopically, exhibits a more dynamic pattern, the main features of which are multicentricity and the appearance of "new" lesions in areas that previously appeared normal. Ewing felt that this represented metastasis in spite of the benign histology. On the other hand, Willis (18), Parsons and Ebbs (10), and Wollstein (17) believe that these multiple angiomas are vascular malformations of congenital origin, which develop independently from vascular tissues that have retained certain embryonal growth characteristics. We believe that this latter concept is more in accord with all of the observed facts.

A surgical specimen may show expansion and thinning of the bone by multilocular cysts. The cysts appear to communicate with each other and are usually filled with clear fluid. A few, particularly those at the periphery of a lesion, contain blood, and are presumably "younger" areas of angiomatous malformation that have retained some of the functional characteristics of

blood vessels. Occasionally no evidence of hemorrhage is present. The cysts contain no trabeculae.

Microscopically, the large cystic spaces are lined by endothelial cells and contain either no blood cells or very few. Near the normal portion of the bone, the cystic spaces become smaller and sometimes take on the appearance of irregularly distributed nests of telangiectases. These smaller cysts and telangiectases are separated from each other by normal marrow and may be engorged with blood. No microscopic features of malignancy have been reported in any of the cases studied.

Radiology: Many radiologic descriptions of hemangioma of bone have been published (1–3, 7, 9). Most frequently recognized are those in the spine, which show increased vertical striation of the vertebral body. In hemangioma of the skull, a well circumscribed area of rarefaction, with a peculiar honeycomb appearance, is usually seen. In flat bones, such as the pelvis or scapula, a sunburst of bony trabeculae extends from the bone into the soft tissues. When cylindrical bones are involved, small loculations containing a fine fibrillary network are seen. Ackermann and Hart (1) stressed the importance of fusiform widening of bone and coarsened trabeculation, which is irregularly arranged and denser than normal. They pointed out, too, that the epiphyseal cartilage is usually spared and that there is no penetration into joints. Early lesions are identified as cyst-like areas of rarefaction. With increasing age, the lesions become sclerotic and trabeculated.

The radiologic appearance of cystic angiomatosis differs from the classical descriptions of skeletal hemangioma in that the lesions are identical regardless of the bone involved (Figs. 1, 3, and 4), and the rounded, cystic spaces show no evidence of fibrillation or trabeculation (Fig. 6). Individual lesions may be unilocular or multilocular and vary in diameter from a few millimeters to several centimeters (Fig. 4). Each is ringed by a sharply demarcated rim of sclerotic bone and there may be a local increase in bone density as though by compression of trabeculae (Fig. 6). There is no evidence of reactive bone formation or periosteal lifting. Involvement of epiphysis, metaphysis, and diaphysis has been reported, but the epiphyseal cartilage is not affected. Some of the lesions occur in the cortex, others in the spongiosa. The larger, more deeply seated lesions have a tendency to expand the bone and thin the overlying cortex. Fractures through the cysts may produce bony deformity (Figs. 3 and 5).

Treatment: There is no report of the use of radiotherapy in cystic angiomatosis. However, deep x-ray therapy has been recommended as the treatment of choice for the usual deep-seated hemangiomas of bone, particularly since surgery may be technically difficult and is often dangerous to the patient because of hemorrhage. Depth dosages of approximately 3,000 r delivered in from three to nineteen weeks have been used successfully (5, 14). Curettage has been employed for accessible, solitary lesions.

Prognosis: The limited number of cases studied makes it difficult to indicate the prognosis. It would seem logical, however, that life expectancy would be more influenced by visceral involvement, which may cause heart failure or hemorrhage and anemia, than by bony lesions, which predispose to multiple fractures.

SUMMARY

A rare form of generalized hemangiomatosis which produces cystic changes in bones, is presented. The bone is weakened locally and fractures may occur. Blood chemical studies are normal. The diagnosis is established by biopsy; excision of a costal lesion is the procedure of choice for this purpose. Deep x-ray therapy is suggested.

ACKNOWLEDGMENT: We are grateful to Mr. William S. Cornwell, Associate in Radiology, University of Rochester, for editorial assistance in preparing the manuscript; to Roger Terry, M.D., Associate Professor of Pathology, University of Rochester, for his help in presentation of the pathological sections, and to Mr. James McElwain, R.T., who made the radiographs.

REFERENCES

1. ACKERMANN, A. J., AND HART, M. S.: Multiple Primary Hemangioma of the Bones of the Extremity. Am. J. Roentgenol. **48:** 47–52, July 1942.
2. ANSPACH, W. E.: Sunray Hemangioma of Bone with Special Reference to Roentgen Signs. J.A.M.A. **108:** 617–620, Feb. 20, 1937.
3. BUCY, P. C., AND CAPP, C. S.: Primary Hemangioma of Bone with Special Reference to Roentgenologic Diagnosis. Am. J. Roentgenol. **23:** 1–33, January 1930.
4. EWING, J.: Neoplastic Diseases: A Treatise on Tumors. Philadelphia, W. B. Saunders Co., 4th ed., 1940.
5. FOSTER, D. B., AND HEUBLEIN, G. W.: Hemangioma of Vertebra Associated with Spinal Cord Compression. Case Report. Am. J. Roentgenol. **57:** 556–561, May 1947.
6. GESCHICKTER, C. F., AND COPELAND, M. M.: Tumors of Bone. Philadelphia, J. B. Lippincott Co., 3d ed., 1949, pp. 612–620.
7. GESCHICKTER, C. F., AND MASERITZ, I. H.: Primary Hemangioma Involving Bones of the Extremities. J. Bone & Joint Surg. **20:** 888–900, October 1938.
8. JACOBS, J. E., AND KIMMELSTIEL, P.: Cystic Angiomatosis of the Skeletal System. J. Bone & Joint Surg. **35-A:** 409–420, April 1953.
9. NEMENOV, M. J.: Roentgen Diagnosis of Hemangioma of the Long Bones. Radiology **33:** 465–469, October 1939.
10. PARSONS, L. G., AND EBBS, J. H.: Generalized Angiomatosis Presenting the Clinical Characteristics of Storage Reticulosis, with Some Observations on the Reticulo-Endothelioses. Arch. Dis. Childhood **15:** 129–158, September 1940.
11. RITCHIE, G., AND ZEIER, F. G.: Hemangiomatosis of the Skeleton and the Spleen. J. Bone & Joint Surg. **38-A:** 115–122, January 1956.
12. SHENNAN, T.: Histologically Non-malignant Angioma, with Numerous Metastases. J. Path. & Bact. **19:** 139–154, 1914.
13. SHERMAN, M.: Capillary Hemangioma of Bone. Arch. Path. **38:** 158–161, September 1944.
14. STOLL, B.: X-Ray and Radium Therapy for Students. London, H. K. Lewis & Co., 1952, p. 123.
15. THOMAS, A.: Vascular Tumors of Bone. Pathological and Clinical Study of 27 Cases. Surg., Gynec. & Obst. **74:** 777–795, April 1942.
16. TÖPFER, D. (1928) as quoted by Jacobs and Kimmelstiel (8).
17. WOLLSTEIN, M.: Malignant Hemangioma of Lung with Multiple Visceral Foci; Report of Case. Arch. Path. **12:** 562–571, October 1931.
18. WILLIS, R. A.: Pathology of Tumors. St. Louis, C. V. Mosby Co., 2d ed., 1953, pp. 700–715.

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SUMMARIO IN INTERLINGUA

Cystic Angiomatosis de Osso

Le autores reporta un caso—secundo lor informationes le prime in le litteratura radiologic—de un forma rar de hemangiomatosis generalisate con alterationes cystic in le ossos. Le osso exhibi indebilitation local, e fracturas pote occurrer. Studios chimic monstra que le sanguine es normal. Le symptomas de presentation pote esser relationate a tumefaction circa un lesion ossee o a un fractura pathologic a transverso un cyste. Illos etiam pote esser secundari a cystic angiomas visceral, con dolores abdominal, ascites sanguinose, tusse, o hemoptysis. Le diagnose es establite per biopsia, preferibilemente de un lesion costal.

Le apparentia roentgenographic del lesiones es le mesme sin reguardo a qua ossos es afficite, e le arrondate spatios cystic non exhibi ulle signo de trabeculation. Cystes individual pote esser unilocular o multilocular, e illos pote variar ab pauc millimetros a plure centimetros in diametro. Illos es incirculate per un nettemente demarcate margine de osso sclerotic, e il pote occurrer un augmento local del densitate ossee como si effectuate per compression de trabeculas. Le plus grande lesiones de sito profunde tende a extender le osso e a tenuificar le cortice exterior.

Roentgenotherapia esseva tentate in le caso del presente reporto, sed resultatos conclusive non esseva obtenite.

Roentgen Manifestations of Congenital Agammaglobulinemia[1]

A. R. MARGULIS, M.D., S. B. FEINBERG, M.D., R. G. LESTER, M.D., and R. A. GOOD, M.D.[2]

AGAMMAGLOBULINEMIA, a relatively new disease characterized by the virtual absence of gamma globulin from the circulation, was first described by Bruton (1) in 1952. His patient showed increased susceptibility to infection, was found to lack gamma globulin on electrophoretic study of the serum proteins, and failed to form antibody in response to antigenic stimulation. Since this initial description, agammaglobulinemia has been extensively studied and numerous cases have been reported (2–10). From present data it would appear that diseases based on failure of gamma globulin synthesis are uncommon but not rare.

It is the specific purpose of this report to describe certain roentgen features of congenital agammaglobulinemia which we believe may, on occasion, contribute to its early diagnosis. In addition, the clinical and laboratory manifestations of the disease will be reviewed briefly. Data to be presented were obtained from a study of roentgenograms taken during the past year of seven patients with congenital agammaglobulinemia.

CLINICAL CHARACTERISTICS OF AGAMMAGLOBULINEMIA

At the present time patients with agammaglobulinemia usually present themselves to the clinician with a history of having suffered for several years from recurrent episodes of life-threatening infection. In many instances the admission history reveals a succession of attacks of pneumonia, meningitis, septicemia, and infections of the middle ear and paranasal sinuses. The curiosity of the physician is finally provoked by these recurrent infections, a deficient immunologic mechanism is suspected, and diagnosis of the disease is made by electrophoretic analysis of the serum. Certainly, as we become more familiar with this disease and more suspicious of its occurrence, diagnosis will be suggested and established earlier in its course, and many of its devastating consequences, including early death and crippling pulmonary disease, may perhaps be avoided.

Agammaglobulinemia has four cardinal features: increased susceptibility to infection, absence of gamma globulin from the blood and tissues, absence of circulating antibody from the blood and tissues, and failure of antibody production in response to antigenic stimulation. Three forms of the disease may be recognized. The form originally described by Bruton is a congenital disease in which the basic disturbance appears to be an inborn error of metabolism transmitted genetically as a sex-linked recessive trait. All patients with this form of the disease have been males, and brothers and maternal male cousins have been involved.

In the acquired form of agammaglobulinemia the patients begin to suffer from recurrent episodes of bacterial infection, after previously normal health. Pneumonia, meningitis, septicemia, skin infections and infections of the middle ear and paranasal sinuses are particularly troublesome. This type of the disease may occur in either sex, and may have its onset at any age.

The third form—isolated agammaglobulinemia—appears to be merely an extension of the normal relationships in gamma globulin metabolism. Transient agammaglobulinemia occurs when the decline in serum gamma globulin concentration which is characteristic of the neonatal

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TABLE I: SEVEN CASES OF CONGENITAL AGAMMAGLOBULINEMIA

Case	Hilar Nodes	Pulmonary Involvement				Sinuses	Adenoids
		Infiltrate	Emphysema	Atelectasis	Bronchiectasis		
B.H.	Absent	Minimal	Moderate	0	0	Mucosal thickening	Absent
F.T.	Absent	Widespread	0	0	0	*	Absent
T.T.	Absent	One lobe	Minimal	0	0	Underdeveloped but not definitely diseased	Absent
T. A.†	Absent	Widespread	0	0	0	*	Absent
W.A.	Absent	?	Compensatory, left lung	Right lung	Marked	Pansinusitis	Absent
J.S.	Absent	One lung	0	0	0	*	Absent
E.S.	Absent	One lobe	Minimal	0	0	Pansinusitis	Absent

* Films not taken. † Large, normal thymus.

period is extended significantly beyond the time at which normal production ordinarily begins and increasing concentrations are observed. Electrophoretic agammaglobulinemia may appear in infants aged six weeks to six months who subsequently form antibodies and gamma globulin in normal amounts. Some of this group, like patients with persistent congenital and acquired agammaglobulinemia, experience recurrent severe bacterial infections during the agammaglobulinemic episode. Recurrent and overwhelming pneumonia and septicemia have been the clinical problem encountered by the present authors.

Extensive immunologic and hematologic investigations in the congenital and acquired forms of agammaglobulinemia have revealed an extreme immunologic deficit which appears to be associated with failure of the reticulum cells (mesenchyme) to differentiate along the plasma-cell line in response to antigenic stimulation (11). Although methods of diagnostic screening for suspected cases of agammaglobulinemia have been suggested (12), the diagnosis must be made by zone electrophoresis, free electrophoresis, or specific immunochemical determination of the gamma globulin concentration. Immunochemical studies performed thus far indicate that in all instances the term agammaglobulinemia is in reality a misnomer, since minute amounts of gamma globulin are detected in the serum by immunochemical studies in all patients, in somewhat larger amounts in those with acquired agammaglobulinemia than in those with the congenital disease (3, 4).

An important paradox in these cases has been the observation, originally reported by Janeway *et al.* (2) and confirmed in our studies (3), that whereas recurrent or persistent bacterial infections are a fundamental feature of agammaglobulinemia, these patients seem to be able to develop immunity to certain virus infections and as a group do not suffer from repeated episodes of this type.

The frequency and distressing nature of the recurrent and persistent pulmonary diseases have been the subject of a separate report (13). Their predominance makes it practically axiomatic that the roentgenologist will be among the first of the physicians to encounter the patient with agammaglobulinemia. In the congenital form, certain roentgenologic features may suggest the diagnosis.

ROENTGEN MANIFESTATIONS

This study is based on findings in 7 male patients with congenital agammaglobulinemia, ranging in age from three months to nine years. All had repeated chest roentgenograms; in at least 1 a nasopharyngeal soft-tissue roentgen study was done, and 4 had x-ray examinations of the sinuses. The findings are summarized in Table I. In all of these cases, diagnosis was established by repeated electrophoretic analyses of the serum, immunochemical determination of serum gamma globulin concentration, and demonstration of the immunologic handicap by studies following extensive attempts at immunization. None of the patients had been subjected to surgical excision of the tonsils or adenoids prior to study.

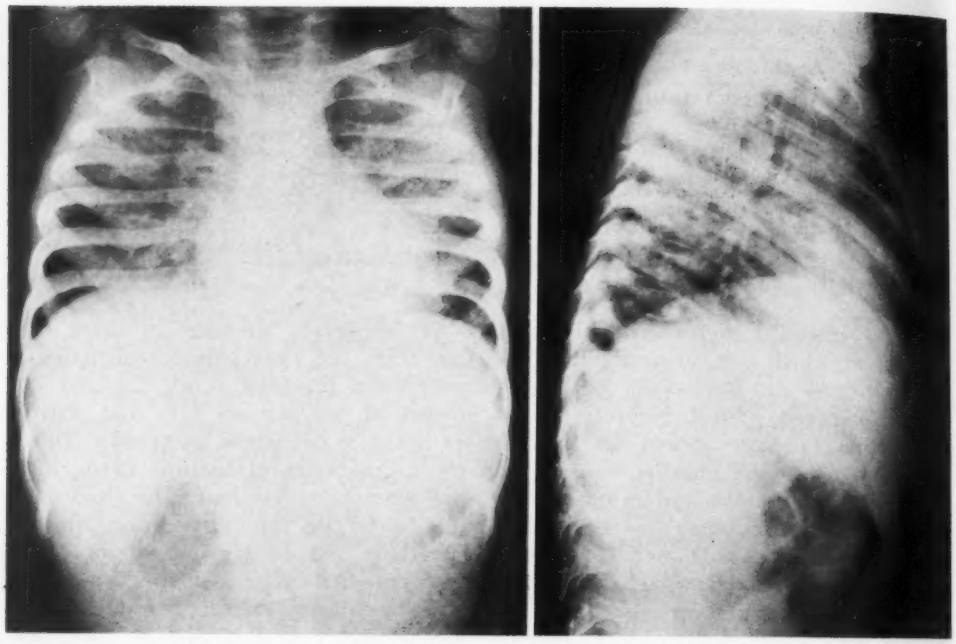


Fig. 1. Frontal and lateral chest films of a two-year-old boy (F. T.), showing widespread chronic pulmonary inflammatory disease, but no lymphadenopathy or peripheral emphysema.

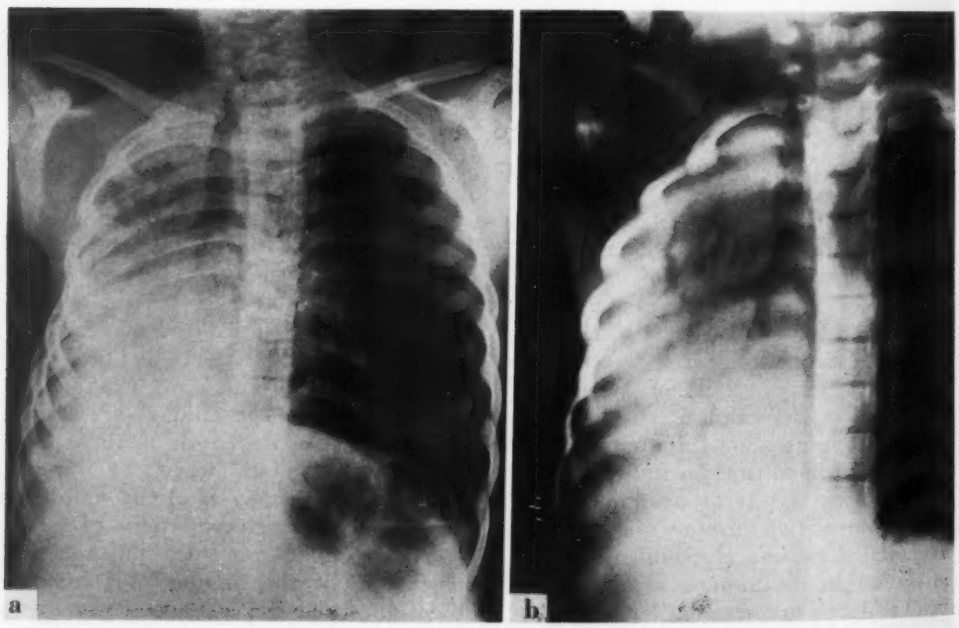


Fig. 2. W. A., eight-year-old boy. A. Atelectasis of the right lung with severe bronchiectasis and compensatory emphysema in the left lung, which is not otherwise involved. Note the lack of lymph node enlargement. B. Frontal planigram of the chest demonstrating the bronchiectasis. There is no extrinsic indentation of the bronchi, as would be seen with lymphadenopathy.

Chest Findings: In spite of pulmonary disease, which was sometimes extensive, hilar adenopathy was not observed (Fig. 1). This was considered a striking observation, since hilar adenopathy is a frequent concomitant of most pulmonary infections in this age group. Its absence is a criterion distinguishing agammaglobulinemia from other chronic widespread diseases involving the lungs. One of the patients had severe bronchiectasis with atelectasis of the entire right lung and marked compensatory emphysema of the left (Fig. 2). It was noted, however, that emphysema was not a significant feature of the disease. It was absent in all patients with widespread pulmonary involvement, and was minimal in 2 cases in which the infiltrates were localized. Obvious bronchiectasis within the atelectatic lung was demonstrated in the 1 patient in whom bronchography was done. Its possible presence cannot be ruled out in the other 6, although it was not suggested by the clinical picture. The thymus shadow was of normal appearance in all cases. Indeed, one child had a fairly bulky thymus (Fig. 3), which was not unusual for his age. The observation that in some children with agammaglobulinemia the thymus is of at least normal roentgenologic dimensions is in keeping with studies in this and other laboratories which dissociate the gland from participation in the immune response (14).

Nasopharyngeal Studies: In all 7 patients lateral views of the nasopharynx were obtained and in all absence of the normal nasopharyngeal lymphoid tissue was demonstrated (Fig. 4,a). This study was prompted by the suggestion of Neuhauser (15) to one of us (R. A. G.) that this abnormality could be used as a screening test for agammaglobulinemia. The striking disparity in appearance from the normal is illustrated in Figure 4. The absence of demonstrable nasopharyngeal lymphoid tissue appears to be a roentgenologic manifestation of the generalized hypoplasia of such tissues in patients with congenital agammaglobulinemia.

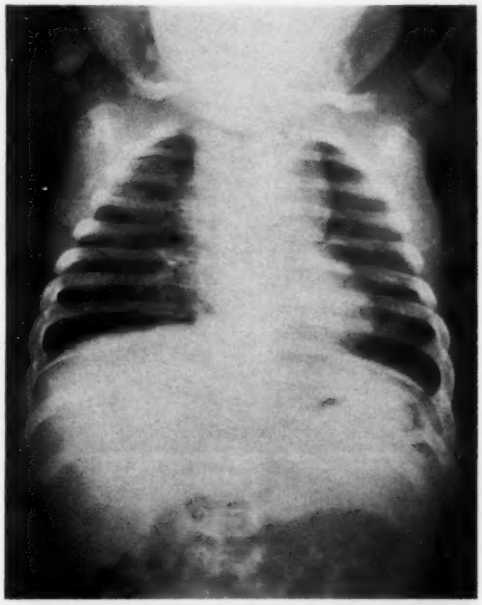
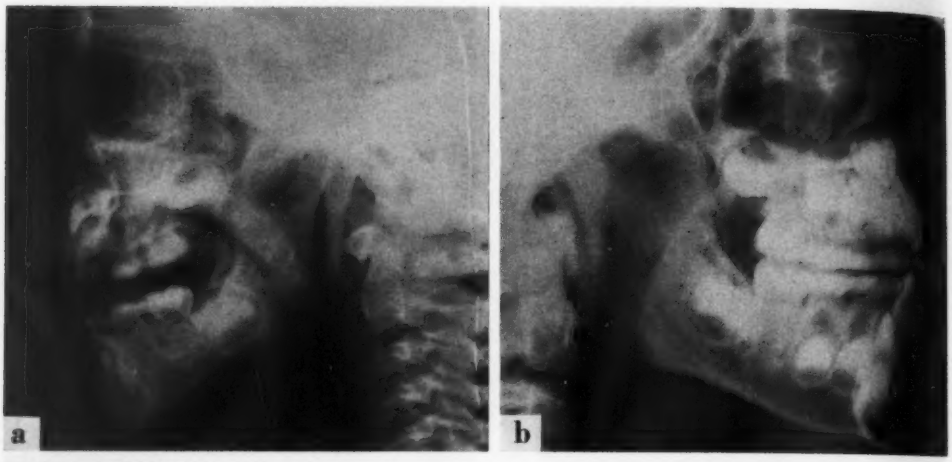


Fig. 3. Frontal chest film of a three-month-old male infant (T. A.), showing infiltration in the right upper lung as well as in the left upper and lower lung. There is a lack of lymphadenopathy, but the thymus is of normal prominence.

Sinuses: Two of the patients had severe pansinusitis, and 1 showed mucosal thickening. We believe this finding in some instances to be due to bacterial infection of the paranasal sinuses and in others to be a non-specific reflection of generalized respiratory disease. The regularity of the occurrence of sinus disease in this small group is a further illustration of the patient's basic inability to cope with bacterial invaders.

DISCUSSION

Congenital agammaglobulinemia is an uncommon disease, which, however, is being recognized with greater and greater frequency. It should always be included in the differential diagnosis of recurrent or chronic lung disease, especially in children. If the observer is aware of this entity, its presence should be suggested by repeated bouts of pulmonary disease without hilar adenopathy and the absence of adenoid tissue on roentgenologic examination. The frequent association of sinusitis reflects



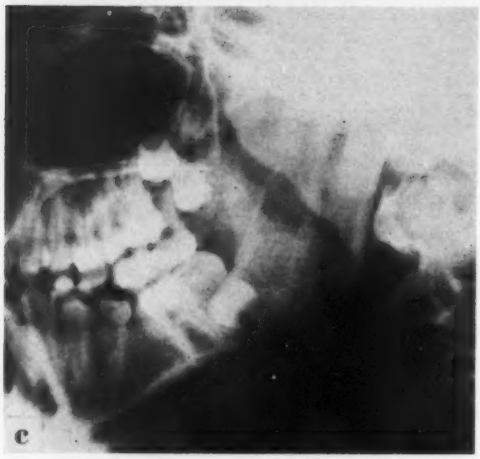


Fig. 4. a. Lateral film of the nasopharynx of a two-year-old boy (J. S.), with congenital agammaglobulinemia, showing absence of normal lymphoid tissue.
b. Film of nasopharynx of a six-year-old boy (F. H.) with congenital agammaglobulinemia.
c. Lateral film of the nasopharynx in a normal child showing normal nasopharyngeal lymphoid tissue.

the generalized nature of the bacterial infections. While it is true that accurate and definitive diagnosis must be made by laboratory and immunologic tests, the roentgen appearance may be sufficiently suggestive to prompt such studies.

SUMMARY

The clinical, diagnostic, and immunologic aspects of congenital agammaglobulinemia are described and several forms of the disease are discussed.

Roentgen features of potential diagnostic importance observed among 7 male children included extensive pulmonary parenchymal disease with paradoxical absence of hilar node enlargement, striking deficiency of nasopharyngeal lymphoid tissue in spite of recurrent upper respiratory tract infection, and frequent sinusitis.

These observations hold only for patients with congenital agammaglobulinemia. In those with the acquired disease, an obverse situation often obtains. The patients may have extensive hypertrophy of the lymphatic tissue, even associated with granulomatous tissue, thus decreasing the value of roentgenography for early recognition of the disease.

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REFERENCES

1. BRUTON, O. C.: Agammaglobulinemia. Pediatrics **9**: 722–727, June 1952.
2. JANEWAY, C. A., APT, L., AND GITLIN, D.: "Agammaglobulinemia." Tr. A. Am. Physicians **66**: 200–202, 1953.
3. GOOD, R. A., AND ZAK, S. J.: Disturbances in Gamma Globulin Synthesis as Experiments of Nature. Pediatrics **18**: 109–149, July 1956.
4. GITLIN, D.: Low Resistance to Infection: Relationship to Abnormalities in Gamma Globulin. Bull. New York Acad. Med. **31**: 359–365, May 1955.
5. YOUNG, I. I., WOLFSON, W. Q., AND COHN, C.: Studies in Serum Proteins: Agammaglobulinemia in the Adult. Am. J. Med. **19**: 222–230, August 1955.
6. KULNEFF, N., PEDERSEN, K. O., AND WALDENSTRÖM, J.: Drei Fälle von Agammaglobulinämie; ein klinischer, genetischer, und physikalisch-chemischer Beitrag zur Kenntnis des Proteinstoffwechsels. Schweiz. med. Wchnschr. **85**: 363–368, April 16, 1955.

7. PORTER, H.: Congenital Agammaglobulinemia: A Sex-linked Genetic Trait and Demonstration of Delayed Skin Sensitivity (Abst.) Am. J. Dis. Child. 90: 617-618, November 1955.

8. SELTZER, G., BARON, S., AND TOPOREK, M.: Idiopathic Hypogammaglobulinemia and Agammaglobulinemia; Review of Literature and Report of Case. New England J. Med. **252:** 252–255, Feb. 17, 1955.

9. GITLIN, D., AND JANEWAY, C. A.: Agammaglobulinemia: Congenital, Acquired and Transient Forms. In "Progress in Hematology," Vol. I, edited by L. M. Tocantins. New York, Grune & Stratton, Inc., 1956.

10. PRASAD, A. S., AND KOZA, D. W.: Agammaglobulinemia. Ann. Int. Med. **41:** 629–639, September 1954.

11. GOOD, R. A.: Studies on Agammaglobulinemia. II. Failure of Plasma Cell Formation in the Bone Marrow and Lymph Nodes of Patients with Agammaglobulinemia. J. Lab. & Clin. Med. **46:** 167–181, August 1955.

12. GOOD, R. A., AND VARCO, R. L.: A Clinical and Experimental Study of Agammaglobulinemia. Journal-Lancet **75:** 245–271, June 1955.

13. GOOD, R. A., AND MAZZITELLO, W. F.: Chest Disease in Patients with Agammaglobulinemia. Dis. of Chest **29:** 9–35, January 1956.

14. MACLEAN, L. D., ZAK, S. J., VARCO, R. L., AND GOOD, R. A.: Thymic Tumor and Acquired Agammaglobulinemia: A Clinical and Experimental Study of the Immune Response. Surgery **40:** 1010–1017, December 1956.

15. NEUHAUSER, E.: Personal communication.

SUMMARIO IN INTERLINGUA

Manifestationes Roentgenographic de Agammaglobulinemia Congenite

Agammaglobulinemia—un morbo relativemente inusual—es characterisate per un augmentate susceptibilitate a infection, carentia de globulina gamma demonstrate per studios electrophoretic del proteinas seral, absentia de circulante anticorpores ab sanguine e histos, e non-formation de anticorpores in responsa a stimulation antigenic. Iste condition occurre in tres formas: (1) Agammaglobulinemia resultante de un innate error de metabolismo e transmittite geneticamente como tracto recessive in chromosomas sexual; (2) agammaglobulinemia de forma acquirite que se disveloppa post un longe periodo de sanitate normal; e (3) agammaglobulinemia de typo transiente que occurre quando le reduction del concentration de globulina seral—occurrente normalmente durante le periodo neonatal—se prolonga significativemente ultra le tempore a que comencia ordinarimente le production normal e a que un augmento del concentration es consequentemente a observar. Patientes con agammaglobulinemia suffre recurrente o persistente infectiones bacterial, sed il pare que illes es capace a disveloppar immunitate contra certe infectiones virusal.

Le characteristicas roentgenographic observate in 7 juveniles mascule, in tanto que illos es potentialmente de signification diagnostic, include extense grados de morbo parenchymal pulmonar con absentia paradoxe de affectiones de nodo hilar, frappante grados de deficientia de nasopharyngee histos lymphoide in despecto de recurrente infectiones del vias supero-respiratori, morbo de aure medie, e frequente occurrentia de sinusitis.

Iste observationes vale solmente pro patientes con agammaglobulinemia congenite.

Effective Irradiation with Radium for Cancer of the Cervix[1]

SIDNEY M. SILVERSTONE, M.D., and JACK L. MELAMED, M.D.

A KNOWLEDGE OF the dose distribution in the volume of tissue irradiated by radium in the treatment of cervical cancer is essential in determining the indications and limitations of radium therapy in the general plan of irradiation for this disease. The purpose of this study is to present this information, in the form of isodose contours for the radium system commonly employed in the Mount Sinai Hospital.

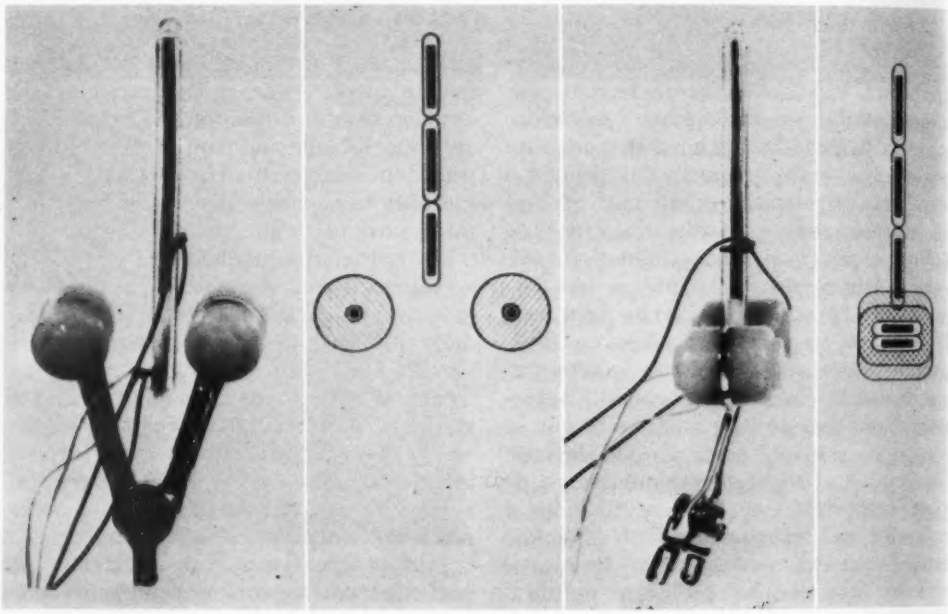

Fig. 1. Radium system: tandem and colpostat.

RADIUM SYSTEM

In the Mount Sinai Hospital, the basic plan of radium therapy of cancer of the cervix uteri consists of the application of a tandem of 3 tubes in the uterine cavity and a colpostat of 2 ovoids in the vaginal vault (Fig. 1). The tandem contains 40 mg. of radium filtered by 1 mm. of platinum and arranged in the 3 tubes in strengths of 15-15-10 mg. from fundus to external os (Fig. 2); its overall active length is 6 cm. The colpostat contains 50 mg. of radium filtered by 1 mm. of platinum, 25 mg. in each ovoid. The transverse ovoid diameter is 2 cm. The ovoids are placed in the lateral fornices, one on each side, and the maximum transverse separation consistent with safe distensibility of the vaginal vault is obtained by means of the special spreading mechanism of the colpostat. The representative point system is employed for the calculations of dosage in the pelvis. The location of the points is illustrated in the diagram. Point A in the paracervical triangle and Point B in the lateral pelvic wall, described originally by Tod and Meredith, are 2 and 5

[1] From the Department of Radiotherapy, The Mount Sinai Hospital, New York, N. Y. Read before the Eastern Conference of Radiologists, New York, March 8, 1957. Accepted for publication in April 1957.

cm., respectively, lateral to the tandem in a plane 2 cm. above the vaginal vault. The other representative points are Point C in the cervix, V in the posterior bladder wall, R in the anterior rectal wall, and F in the head and neck of the femur.

The geometric arrangement of the radium is considered ideal when the tandem is in the sagittal plane with its active end in line with the vaginal vault (Fig. 3) and the ovoids of the colpostat are symmetrically placed in the lateral vaginal fornices

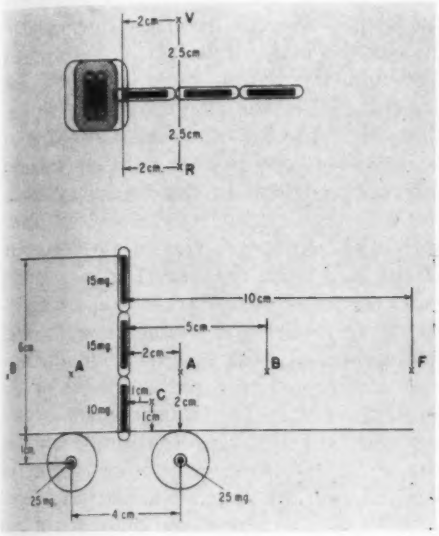

Fig. 2. Basic plan: radium geometry and representative point system.

in the transverse plane. For the special purposes of this study we elected to construct isodose curves through three points: the first, Point A in the paracervical triangle, the second, Point B in the lateral pelvic wall, and the third, a point in the parametrium that represents mid-value in dosage between Points A and B. The practical significance of these isodose contours will become apparent as the results of this investigation are presented.

PHOTOGRAPHIC METHOD

The photographic method described by Loevinger and Spira was employed to construct the isodose contours. In this method,

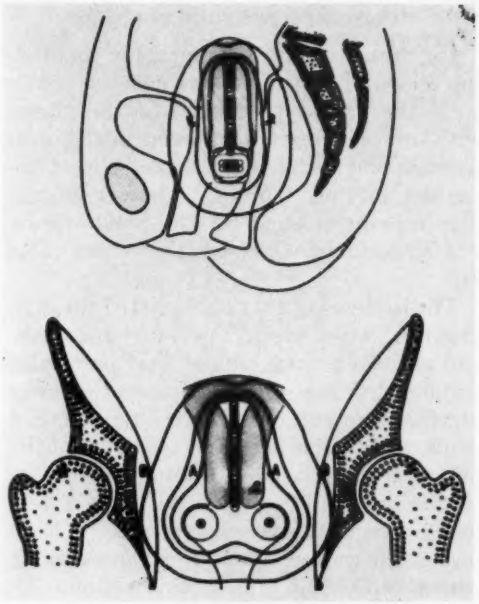

Fig. 3. Ideal arrangement of tandem and colpostat; location of representative points; isodose-contour volumes.

slow-acting (Adlux) film is exposed to the radium in the tandem and colpostat placed in a Presdwood phantom, so as to reproduce the actual conditions in the female pelvis. Within a certain range, determined by Loevinger, the resultant photographic densities bear a linear relationship to the radium exposure and are therefore quantitatively comparable to actual dosage.

By means of a densitometer, the photographic densities at Points A and B and at the point midway between them in density value may be traced on the exposed film, and the isodose contours thus constructed. In the construction of isodose contours in the sagittal plane, the density values obtained in the transverse plane were used so that the contours in both planes corresponded to the same dosage values. In all experiments, the films were taken from the same batch, exposed to the radium for the same length of time (three hours and twenty minutes) and developed together in order to maintain constancy of photographic technic.

THE ISODOSE CONTOUR VOLUMES

By means of the photographic method, the 3 isodose contours were constructed in both the transverse and sagittal planes with the tandem and colpostat in the ideal position and with a 4-cm. separation of the vaginal radium sources. These contours may now be studied for the pelvic tissue and structures included within them (Fig. 3).

The isodose contour constructed through Point A, when viewed in both transverse and sagittal planes, defines that particular volume of tissue which comprises the lower uterine segment and cervix, the vaginal vault, and the paracervical segments of the parametria, that is, a volume which includes practically all of the Stage I and many Stage II cervical cancers. Therefore, if the dose at Point A is cancerocidal, which is feasible, the entire volume defined by the above isodose contour receives the cancerocidal dose from the radium alone.

The isodose contour through Point B includes the parametria and an appreciable segment of the lateral pelvic wall, most of the vagina, the posterior wall of the bladder, and the anterior wall of the rectum. This volume comprises many of the Stage III and some of the Stage IV cases of cancer. The radium dose at Point B, which can be easily calculated, therefore represents the dose to this large volume of tissue. It is usually between 30 and 40 per cent of the dose at Point A.

The isodose contour through the point intermediate between Points A and B comprises most of the parametria, a segment of the posterior bladder wall in the region of Point V, and a segment of the anterior rectal wall in the region of Point R. This volume includes nearly all of the Stage II cases. The special significance of this intermediate isodose contour is that it defines a volume of tissue in which only a relatively small amount of supplementary external radiation, 2,000 to 2,500 r, is needed to bring the dose up to the value at Point A.

Thus the isodose contours through Points A and B, and the intermediate point define certain specific dosage volumes, characteristic for the radium system and particularly related to the stage of the disease. These contours define, also, both the indications and the limitations of radium therapy for cancer of the cervix.

SYMMETRICAL SEPARATION OF THE OVOIDS

With the tandem and colpostat in the ideal position, the degree of separation of the ovoids depends upon the distensibility of the vaginal vault. Isodose contours were constructed in both transverse and sagittal planes for vaginal radium separations of 2, 4 and 6 cm. As the separation is increased, the isodose contour volumes increase in width in the transverse plane but become smaller in the sagittal diameter. The greater transverse diameter of the A isodose contour (Fig. 4) includes more of the parametria but its correspondingly narrower diameter in the sagittal plane may be smaller than the normal anteroposterior measurement of the vaginal vault. The intermediate isodose contour volume represents a more desirable distribution of dosage when the vaginal radium sources are widely separated. In the transverse diameter of this contour, the parametria are included to the lateral pelvic wall, while sagittally, the doses to the bladder and rectum can be kept within safe limits. The B-isodose contour volume is not only wider in its transverse diameter but it also includes a greater area of the lateral pelvic wall. An additional advantage of the greater separation and lateral spread of the ovoids in the vaginal vault is the increased dose in the areas defined by the intermediate and B-isodose contours, relative to the A-isodose contour volume. As the separation increases from 2 to 4 to 6 cm., the relative "B" dose increases from 30 to 33 to 40 per cent of the "A" dose, while the "intermediate" dose increases from 65 to 67 to 70 per cent.

VARIATIONS FROM THE IDEAL ARRANGEMENT OF RADIUM

While the radium system consists essentially of the application of a tandem and colpostat, the geometric arrangement of the radium sources will be determined by many anatomic and pathologic conditions, such as: the position of the uterus in the pelvis; the size and shape of the uterine cavity as affected by fibroids, congenital abnormalities, or the neoplasm; the size and distensibility of the vagina and vaginal vault; and the numerous distortions caused by bulky neoplastic masses, ulceration, infection, and tissue breakdown. Since the ideal arrangement of tandem and colpostat is seldom obtained, it was part of our experiment to study the effect on the isodose contours caused by variations from the ideal. For purposes of clarity these variations were analyzed systematically in groups. Points A, B, and that of the intermediate value can no longer be defined when the tandem and colpostat do not conform to the ideal arrangement in the pelvis. Therefore, the film density values for these points were obtained from the ideal arrangement and were used for the isodose tracings in the variations. The resultant isodose contours thus represent what happens when the radium arrangement varies from the ideal.

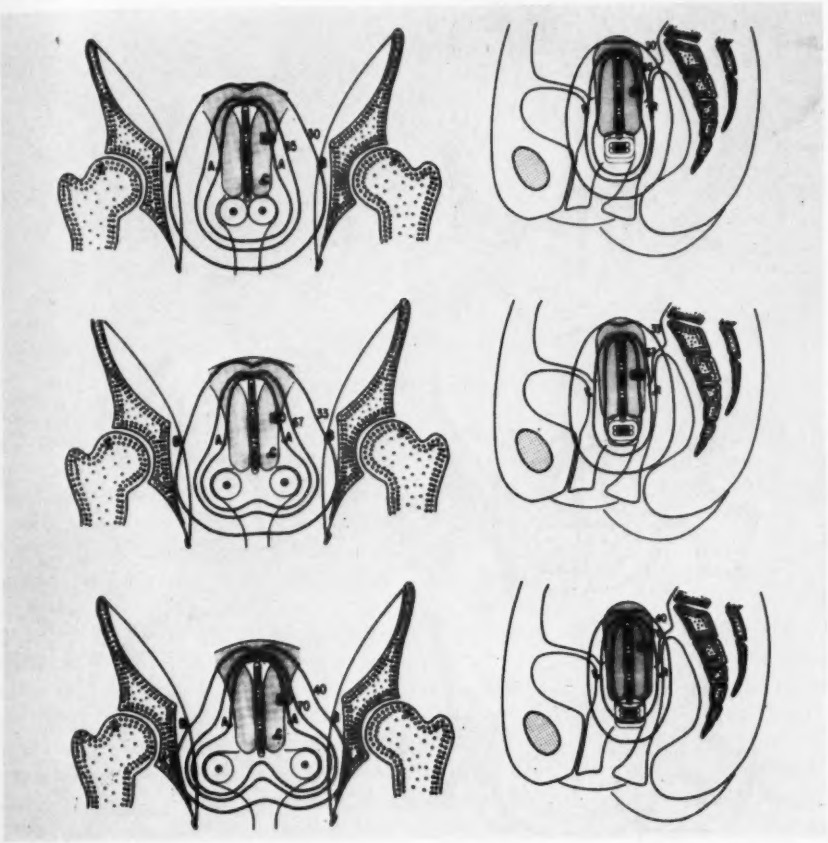

Fig. 4. Effect of separation of ovoids on dosage in irradiated pelvic structures.

Variations of Position of Tandem in Uterus: With the ovoids in constant po-

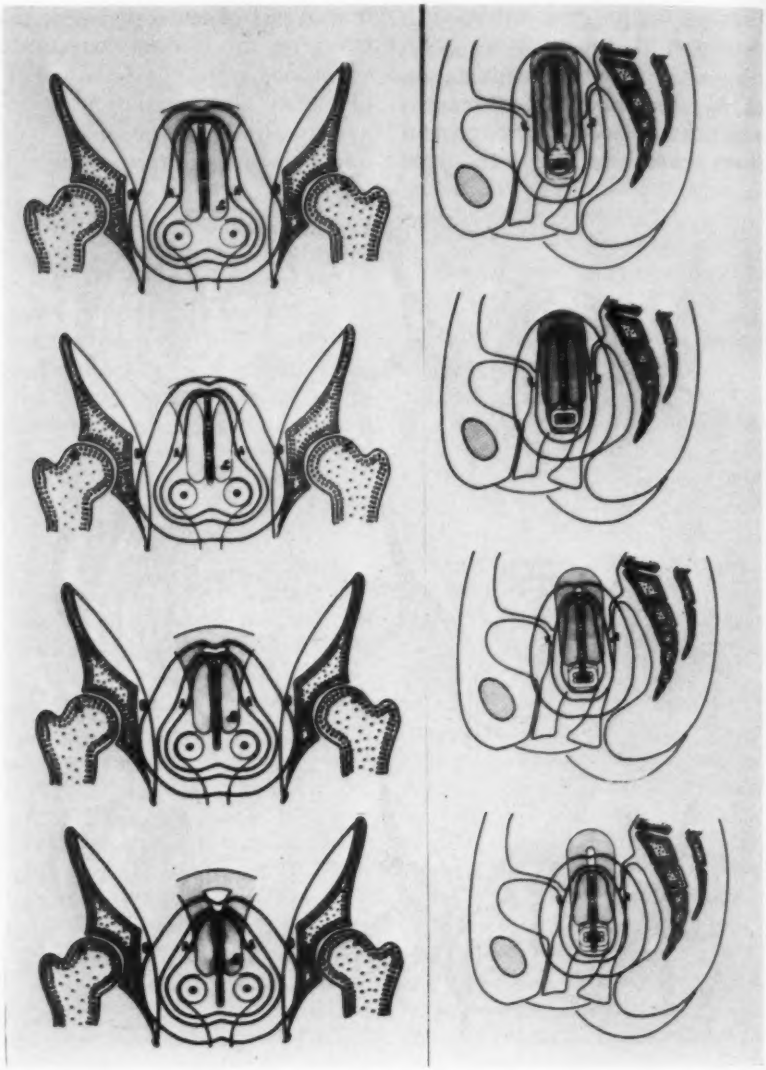

Fig. 5. Variation of position of tandem in uterus.

sition at 4-cm. separation in the vaginal vault, isodose contours in both transverse and sagittal planes were constructed for variations in the tandem position from a high location in the uterine cavity to a low placement in which the tandem protruded partially into the vagina (Fig. 5). The studies demonstrate that the isodose contours follow the position of the tandem and that the irradiation of the uterus is limited to the height of the tandem in the uterine cavity. As the tandem slips downwards into the vagina, more of the vagina is included in the irradiated volume but the transverse diameters of the isodose contours are only slightly widened. In the sagittal plane, the anteroposterior diameters of the isodose contours are narrow when the tandem is in the high intrauterine position and gradually become appreciably wider as the tandem moves downward between the ovoids into the

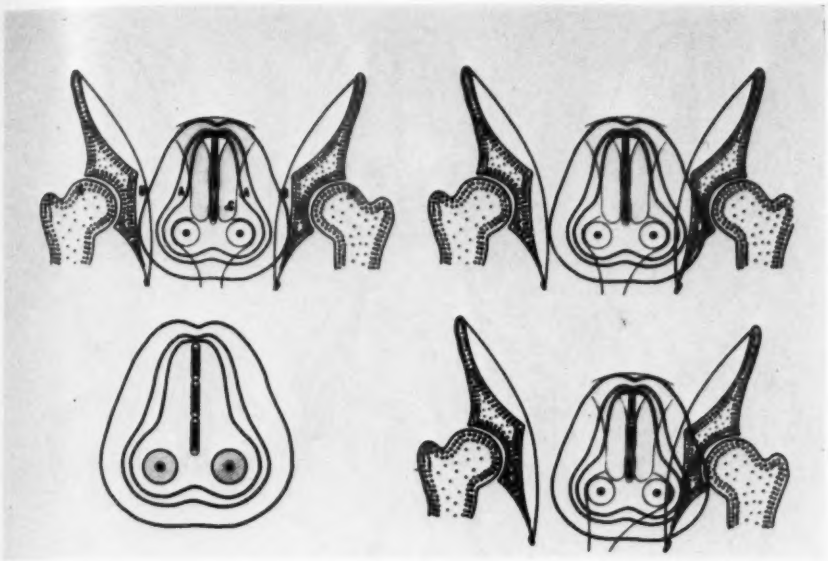

Fig. 6. Lateral shift of radium system.

vaginal canal. With the tandem in high position, the A-isodose contour volume does not include the anterior and posterior fornices of the vaginal vault, while with a very low position of the tandem, the bladder and rectal doses may be higher than is desirable. The position of the tandem in the uterus is therefore of vital importance in estimating dosage to the mid-line structures.

Lateral Shift of Radium System: With the tandem and colpostat in the ideal arrangement, the whole radium system as one unit may shift laterally as a result of a lateral displacement of the uterovaginal axis (Fig. 6). Such a lateral shift may be due to shortening of the parametrium on the side of the shift, as a result of scarring from previous surgery or inflammation, or it may be caused by a bulky mass in the opposite parametrium displacing the cervix laterally. The isodose contours follow the radium sources. Therefore, the uterovaginal structures normally included within these contours are basically unchanged since the anatomical relationships of the uterus, vaginal vault, and paracervical segments of the parametria are maintained. On the other hand, the lateral pelvic wall on the side of the shift will be more heavily irradiated, while on the opposite side the amount of radiation directed to the lateral segment of the parametrium and to the lateral pelvic wall may be too small to be of value.

Lateral Shift of Tandem or Colpostat: With a lateral shift of the tandem or colpostat, the isodose contours undergo a change that follows closely the altered position of the radium sources (Fig. 7). It is as though the isodose contours consisted of a vertical tandem segment and a horizontal colpostat segment shifting in relative position to conform to the new arrangement of the radium. The structures in the uterovaginal axis are included within the A-isodose contour but there is a marked difference in the irradiation of the lateral parametria and pelvic walls on the two sides. With the tandem in the mid-line and the colpostat shifted laterally, the lateral parametrium and pelvic wall on the side of the shift are more heavily irradiated, while on the opposite side the dose fall-off is so rapid that these structures are inadequately irradiated. With the colpostat in mid-pelvic position and the tandem shifted laterally, better symmetry

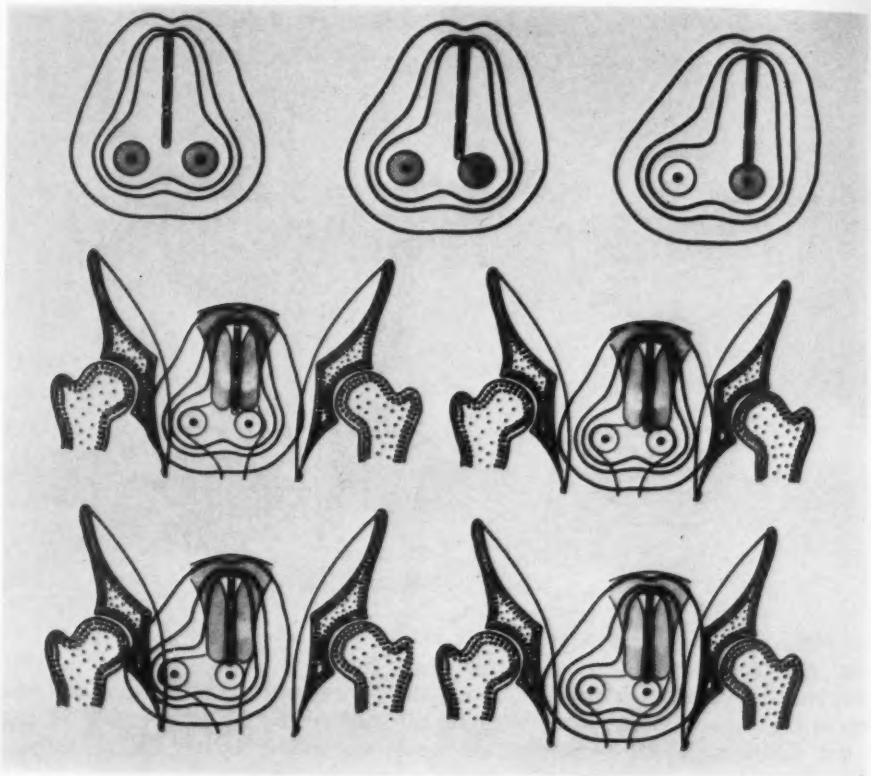

Fig. 7. Lateral shift of tandem or colpostat.

of dose is maintained in the lateral parametria and pelvic walls, but with a significant increase of the dose and included area in the pelvic wall on the side of the shift.

Lateral Angulation of Radium System: With the tandem and colpostat in the ideal arrangement, the whole radium system as one unit may angulate toward one side of the pelvis (Fig. 8). With this type of angulation, however, the isodose contours are not altered, although their position in the pelvis is changed. Since the normal anatomical relationships of uterus, vaginal vault, and paracervical segments of the parametria are maintained even though the uterovaginal axis is angled, these structures are included within the isodose contour volumes as they would be in the ideal position. The lateral parametrium and pelvic wall on the side of the angulation, however, will be more heavily irradiated than on the opposite side.

Lateral Angulation of Tandem: With the colpostat in constant transverse position in the vaginal vault, lateral angulation of the tandem causes a distortion of the isodose contours which follow the new arrangement of the radium sources (Fig. 9). Generally, angulation of the tandem is caused by angulation of the uterus itself and only rarely by an anatomic abnormality or abnormal intra-uterine mass. In most cases, therefore, the uterovaginal axis structures, distorted as they may be, are included within the isodose contour volumes. The irradiation of the lateral parametria and pelvic walls is favored on the side of the angulation. However, with excessive lateral angulation of the tandem, there may be a shift of the colpostat to the opposite side. Such an arrangement of

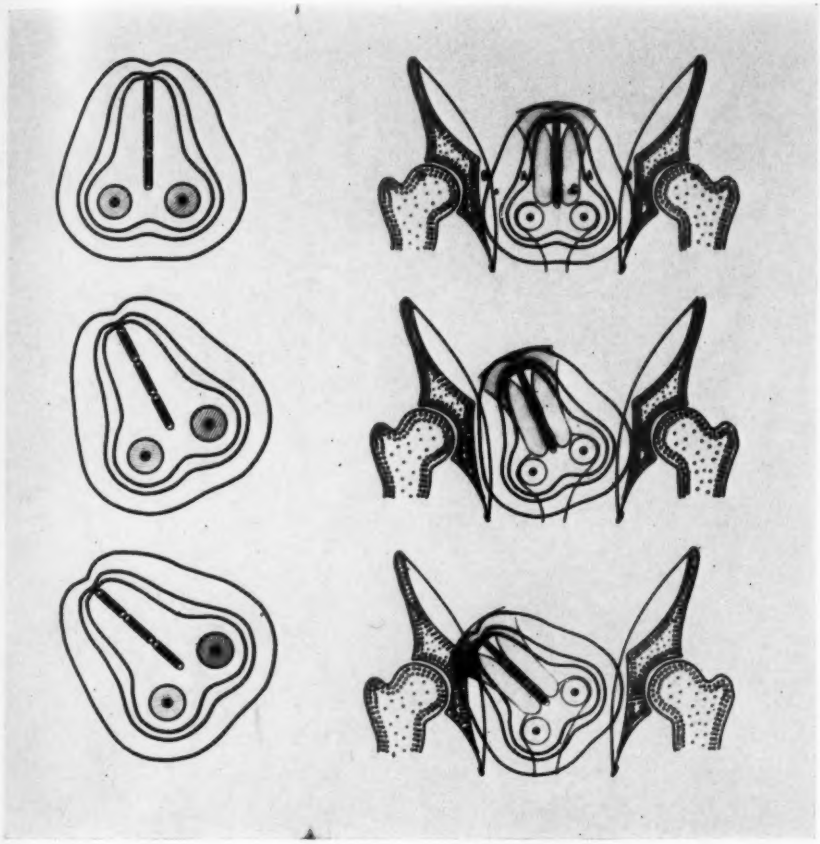

Fig. 8. Lateral angulation of radium system.

radium is favorable for irradiation of the parametria and lateral pelvic walls on both sides.

Angulation of Colpostat: Not infrequently the vaginal vault is so distorted that the ovoids cannot be placed or maintained in a transverse position, or the vaginal vault may be too small to accommodate both ovoids side by side. The result is that one ovoid is at a higher level than the other, the colpostat itself being angulated. With the tandem in the sagittal position and the colpostat angulated, there are corresponding changes in the isodose contours (Fig. 10). The effect of this type of angulation is mainly to reduce the transverse diameter of the isodose contours, but more of the lower vagina is included in the sagittal plane. The structures of the uterovaginal axis are included within the A isodose contour and are therefore adequately irradiated. The lateral parametrium and pelvic wall on the side of the higher ovoid are included within the isodose volumes, but on the side of the lower ovoid the lateral parametrium and pelvic wall may remain outside because of a change in direction of the isodose contours toward the lower vaginal instead of toward the lateral structures.

DISCUSSION

Probably many variations of tandem and colpostat other than those considered above may be encountered in the radium therapy of cancer of the cervix. Complex combinations of lateral shift of tandem or colpostat with angulation of either one or

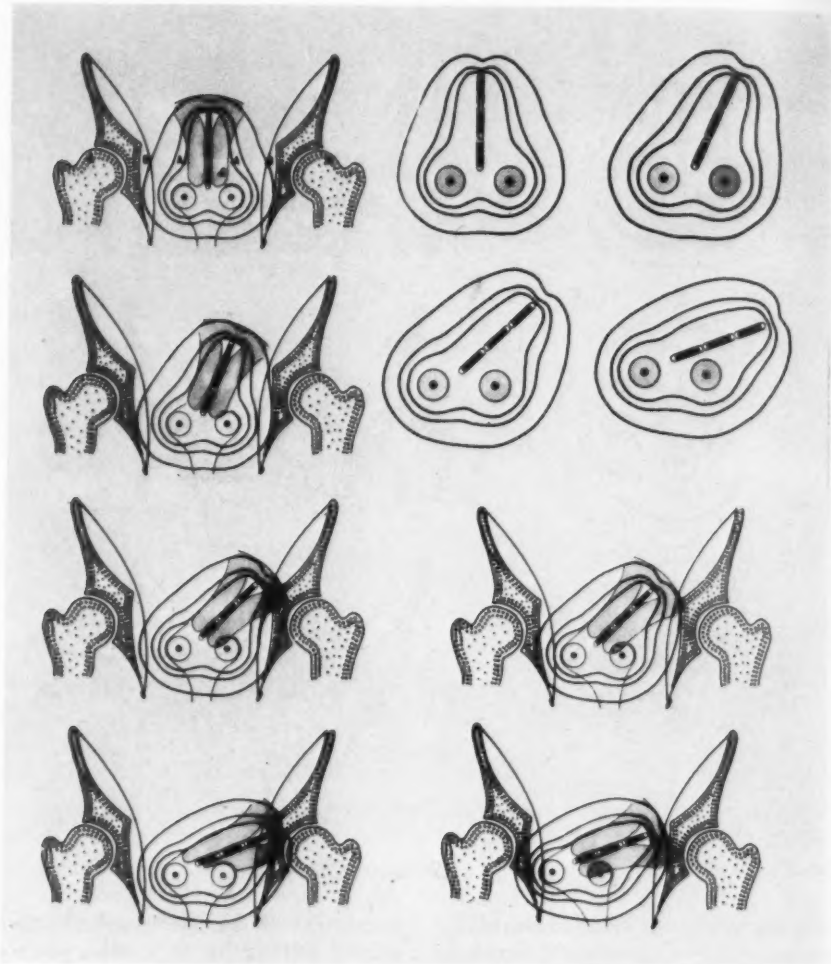

Fig. 9. Lateral angulation of tandem.

both may occur. The groups of arrangements already described comprise most of the variations. Others may be ascertained by interpolation. Essentially the isodose contours follow the geometric outline of the radium sources fairly closely. Since the radium sources are contained within the uterus and vaginal vault, the A-isodose contour includes the lower uterine segment and cervix, the vaginal vault, and part of the paracervical segment of the parametria in practically all of the variations. Because the radium is in the uterovaginal axis, this relationship holds even with a marked shift or angulation of the radium applicators; it is not dependent upon the location of this axis in the pelvis. In contrast, the segment of lateral parametrium and pelvic wall included within the B-isodose contour depends upon the proximity of the radium sources to this part of the pelvis and is greatly influenced by lateral shift and angulation. The intermediate isodose contour, which represents the volume of tissue that can be adequately irradiated with a reasonable degree of certainty in most instances, includes nearly all of the Stage I and Stage

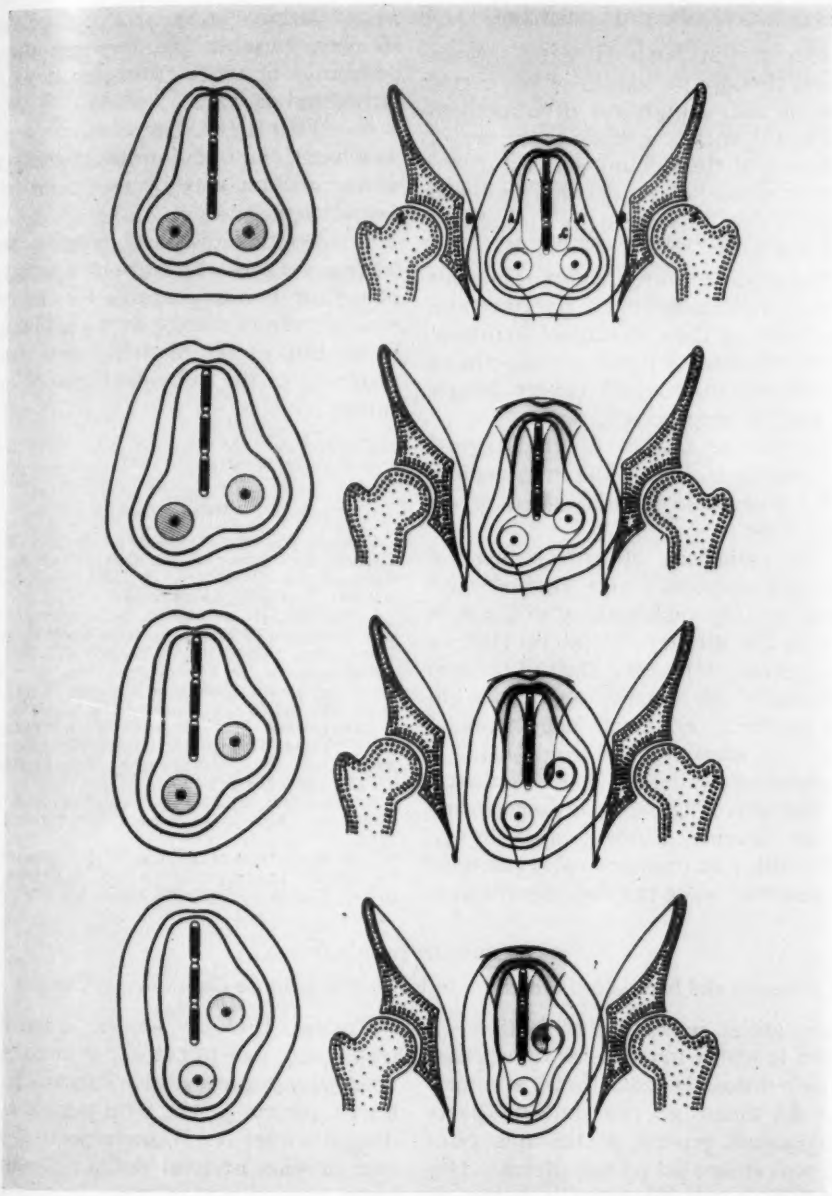

Fig. 10. Angulation of colpostat.

II and some of the Stage III cancers of the cervix in almost all of the variations in arrangement of tandem and colpostat that have been studied.

In practice, it would be best to have the various isodose contour diagrams as readily available as any other table of useful data. From this information, the radium dosage can be correlated with the amount of supplementary radiation necessary to complete the radiation program for any individual case of cancer of the cervix.

SUMMARY AND CONCLUSIONS

1. The Mount Sinai Hospital system of radium therapy for cancer of the cervix consists of the application of a tandem and colpostat with a specific geometry of arrangement of the radium sources.

2. The pelvic dose distribution from the radium can be studied by the photographic method.

3. The isodose contours through Point A, Point B, and a point in the parametrium midway between these in respect to dosage represent volumes of tissue corresponding approximately to cervical cancer Stages I, III, and II, respectively.

4. As the separation of the vaginal radium sources increases, the intermediate and "B" doses also increase relatively to the "A" dose.

5. The variations of arrangement of tandem and colpostat were studied with reference to: (*a*) variations of position of tandem in the uterus; (*b*) lateral shift of radium system; (*c*) lateral shift of tandem or colpostat; (*d*) lateral angulation of radium system; (*e*) lateral angulation of tandem; (*f*) angulation of colpostat. It was demonstrated that the isodose contours follow the uterovaginal axis, comprising the lower uterine segment and cervix, vaginal vault, and paracervical segment of the parametria, while the dose distribution to the lateral parametria and pelvic wall is more variable and depends upon the proximity of the uterovaginal axis to the lateral pelvic wall.

6. With the isodose contours described as a basis, contours for other arrangements of the radium may be ascertained by interpolation.

7. A set of diagrams representing the isodose contours for various arrangements of radium is indispensable for the correlation of radium dosage with supplementary irradiation in the planning of a radiation program for the individual case of cervical cancer.

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REFERENCES

HARRIS, W., AND SILVERSTONE, S. M.: Radiation Therapy for Cancer of the Cervix with Analysis of Fundamental Dosimetry. J. Mt. Sinai Hosp. **14**: 369–382, September-October 1947.

LOEVINGER, R., AND SPIRA, J.: Dosimetry of Multiple Radiation Fields by Superposition of Photographic Films. Am. J. Roentgenol. **77**: 869–872, May 1957.

SILVERSTONE, S. M.: Calculations of Dose from Point and Linear Sources of Radium. Am. J. Roentgenol. **55**: 203–211, February 1946.

SILVERSTONE, S. M., HARRIS, W., AND GREENBERG, M.: Radium Therapy for Cancer of the Cervix Uteri with a New Type of Colpostat. Am. J. Roentgenol. **67**: 294–299, February 1952.

SILVERSTONE, S. M.: A New Improved Type of Colpostat. Am. J. Roentgenol. **73**: 481–483, March 1955.

TOD, M. C., AND MEREDITH, W. J.: Dosage System for Use in Treatment of Cancer of Uterine Cervix. Brit. J. Radiol. **11**: 809–823, December 1938.

SUMMARIO IN INTERLINGUA

Efficacia del Irradiation a Radium in le Tractamento de Cancere del Cervice

Cognoscentias in re le distribution del dosage in le histos irradiate es indispensabile in determinar le indicationes e le limitationes del therapia a radium como parte del programma general de therapia radiational pro cancere del cervice uterin. Iste information es presentate in le forma de profilos isodosal pro le systema a radium que es communmente empleate al Hospital Mt. Sinai a New York. Le systema consiste de tres tubos in tandem in le cavitate uterin e un colpostato de duo ovoides in le fornice vaginal. Un methodo photographic esseva usate pro determinar le distribution del dosage in le pelve.

Curvas isodosal esseva construite a transverso tres punctos: Puncto A in le triangulo paracervical; Puncto B in le lateral pariete pelvic; e un puncto a medie distantia inter A e B con respecto al dosage. Iste profilos isodosal defini volumines de histo que—a parlar generalmente—includerea canceres cervical del stadios I, III, e II, respectivemente. Le valores de dosage indicate per le profilos isodosal passante per le puncto intermediari e per le puncto B accresce in relation al valor representate per le profilo passante per le puncto A in tanto que le separation del fontes de radium in le vagina es augmentate.

Deviationes ab le arrangiamento ideal del fontes de radium occurre frequentemente in le practica. Iste problema es discutite in detalio. In omne casos, le profilos isodosal seque satis strictemente le contorno geometric del fonte de radium, i.e. le axe uterovaginal que comprende le segmento inferior e le cervice, le fornice vaginal, e le segmento paracervical del parametrios. Le distribution de dosage in le parametrios lateral e le pariete pelvic es plus variabile, in dependentia del proximitate del axe uterovaginal al lateral pariete pelvic.

Un batteria de diagrammas representante le profilos isodosal pro varie arrangiamentos del radium es indispensabile in le correlation del dosage de radium con irradiation supplementari in un caso individual de cancere cervical.

Changes in Lung and Pleura Following Two-Million-Volt Therapy for Carcinoma of the Breast[1]

DORIS BATE, M.D.[2] and RUTH J. GUTTMANN, M.D.

A SERIES OF 50 patients treated on the 2-million-volt unit at the Francis Delafield Hospital (New York) between January 1951 and January 1956 were studied with a view to determining the incidence and nature of post-irradiation changes in the lungs and pleura. The patients selected for the investigation all received the same type of radiotherapy, followed by clinical observation for at least six months. In each case a suitable sequence of chest radiographs was available and the roentgen findings were verified by surgical exploration, thoracentesis, or postmortem examination. Changes in the underlying lung were detected roentgenographically in 40 patients, with a single exception within one year after the completion of radiotherapy.

It is felt to be of interest to determine whether such changes represent radiation pneumonitis and eventual fibrosis or are due to metastatic pulmonary disease. It was in the hope that satisfactory diagnostic criteria could be established that these 50 cases, meeting rather rigid requirements as to treatment fields and follow-up, were carefully studied. In addition, an attempt was made to correlate the clinical symptoms with the roentgen findings.

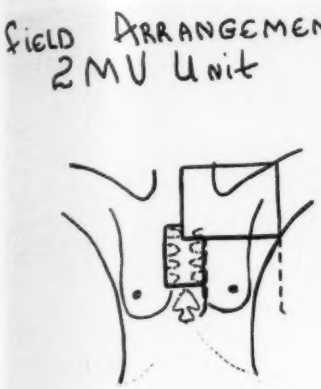
The radiation in these cases was delivered to an anterior field including both supraclavicular and infraclavicular areas and an internal mammary field. The tumor dose was taken at the level of the supraclavicular, axillary, and internal mammary lymph-node chains at 3 to 5 cm. from the surface, depending upon the physical structure of the patient. These limits have been established by surgical exploration in a large number of cases. The field arrangement is shown in Figure 1. The supraclavicular and infraclavicular port includes the axilla and in the average patient measures 15 × 18 cm. The second field is directed to the internal mammary nodes on the involved side and averages 12 × 8 cm.

In some patients of this group tangential fields were added to those just described. These portals extend from the lateral border of the internal mammary field to the posterior axillary line. With this approach the dose to the chest wall is reduced to three-fifths of the tumor dose, while the lung does not receive any appreciable amount of radiation (Fig. 2). Daily dosage and physical factors were constant in the entire group. All patients received a daily tumor dose of 200 r to each of the fields for a weekly dose of 1,000 r. The treatments were given with the 2-million-volt unit, at a target-skin distance of 100 cm., with a half-value layer of 7 mm. of lead. The total overall dose varied: early in the series irradiation was discontinued when a tumor dose of 3,000 r to each area as above had been attained; later the dosage was raised to 5,000 r (tumor dose) delivered in five weeks. The tumor dose given to the majority of the patients ranged between 3,000 and 5,000 r to each of the areas, administered at the rate of 1,000 r per week. In a few of the series therapy had to be interrupted, and these therefore received a somewhat larger over-all dose, one as high as 5,750 r to each of the areas, which, however, was spread over eight weeks. With these dosages delivered at the level of the lymph nodes, the lung at a depth of 10 cm. received only two-thirds of the stated dose.

It has been established that there may be considerable difference between the actual dose distribution in the patient and

[1] From the Francis Delafield Hospital, Columbia University College of Physicians and Surgeons, New York, N. Y. Accepted for publication in April 1957.

[2] Now connected with the Department of Radiology of the Roosevelt Hospital, New York, N. Y.



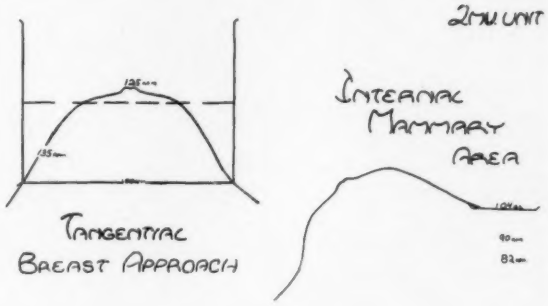


Fig. 1 (left). Anterior field arrangement.
Fig. 2 (right). Dosage distribution when tangential breast fields are added.

the calculated isodose pattern determined from measurements in a water phantom. Ionization measurements were therefore made[3] in a heterogeneous phantom constructed to simulate more closely the actual variation in tissue density in the body. The special phantom consisted of a skeleton and a low-density material (0.32 gm./c.c.) as a substitute for lung tissue. The ratio between the dose measured in this phantom and the dose measured in the water phantom was determined for a 15 × 15-cm. supraclavicular and infraclavicular field and for a 10 × 8-cm. internal mammary field.

For the 15 × 15-cm. field the ratio in the center, at a depth of 4.6 cm., was 1.02: for the 10 × 8-cm. field the ratio, 2 cm. lateral from the sternum, was 1.04 for a depth of 3.7 cm. and 1.08 for a depth of 10.3 cm., thereby indicating the increase in dose due to the low density of the lung material.[4]

As stated above, changes in the underlying lung were demonstrable in 40 of the 50 patients. In 35 of this number the course of events permitted a definite diagnosis of post-radiation effect. In the 5 remaining patients there was proof of pulmonary metastases, although concurrent radiation changes could not be excluded, as will be explained later.

In 7 patients pulmonary symptoms developed between two and six months after completion of therapy: dry cough in 5 patients, dyspnea in 3, and chest pain in 1. The symptoms subsided, as a rule, after three months.

Because of the location of the treatment fields, the upper lobe, mediastinum, and hilus of the treated side showed roentgen findings which in our experience are quite typical. Often the first such change noted would be a diffuse haze over the upper lung field, having the appearance of either pleuritis or pneumonitis. This would be observed from a few weeks to a few months after the conclusion of radiotherapy (Fig. 3,A). It would be followed in one to three months by linear, fibrotic, strand-like densities extending outward and upward from the hilus to the apex (Fig. 3,B). This picture was usually accompanied by shrinkage of the upper lobe, as evidenced by its smaller-than-normal size, deviation of the trachea to that side, and elevation of the hilus and hemidiaphragm. Often the shrinkage and fibrosis would progress for several months and then remain stationary or resolve completely (Fig. 3,C). The case shown in Figure 4 is illustrative of a slight variation in the roentgen features, but with similar, complete resolution within a year. At the time of this report the radiation changes in 5 of the 35 cases had

[3] By Mr. Carl B. Braestrup and Mr. R. Mooney of the Physics Department of the Francis Delafield Hospital.

[4] A separate investigation of this problem was made in relation to cobalt teletherapy. The results will be published in a separate report.

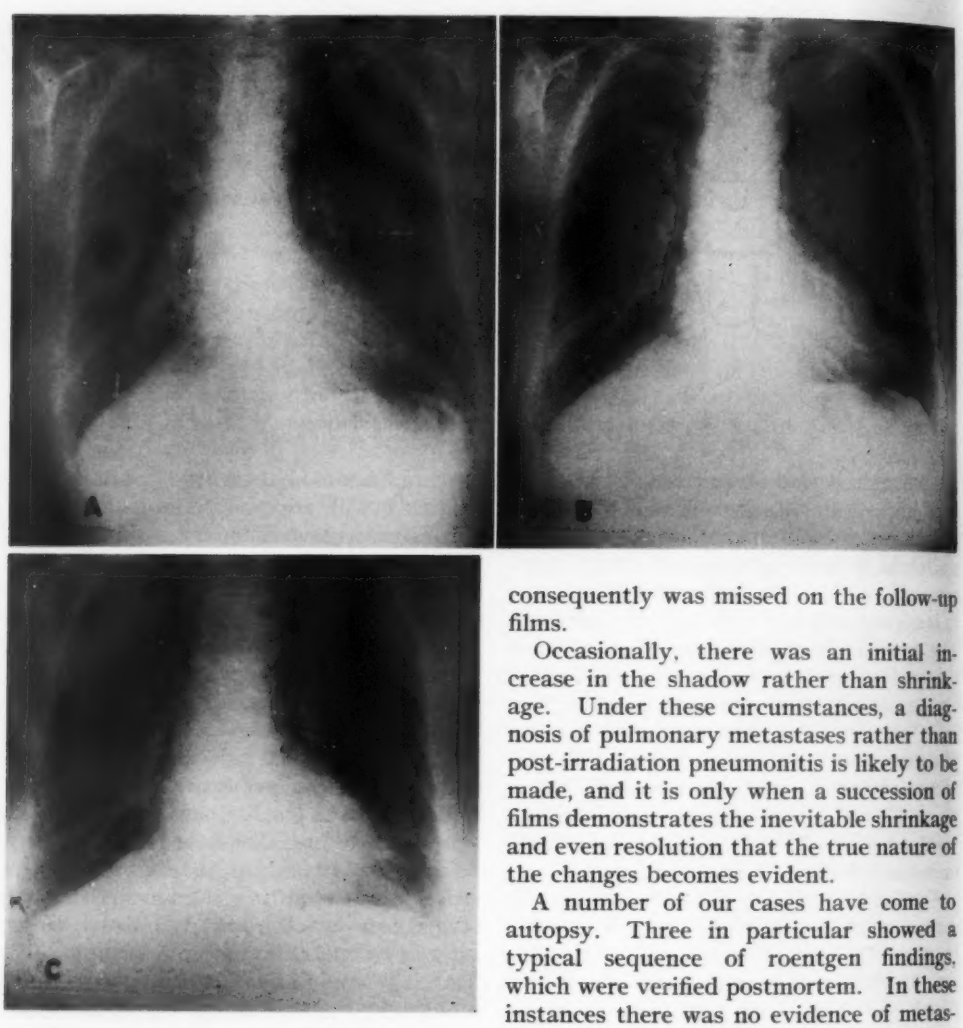


Fig. 3. A. July 30, 1954. Haze over right upper lung field, representing first change, three months after completion of irradiation.
B. Sept. 14, 1954. Fibrotic, strand-like densities extending from hilus to apex, indicating the second phase of postirradiation change.
C. March 30, 1955. Resolution.

resolved or were in the process of resolution, after eight months to one and a half years.

There were many cases in which examination, even as early as three weeks following completion of radiotherapy, failed to show a diffuse pneumonitis and demonstrated only the stage of fibrosis. It must be that in these cases the first stage occurred earlier, perhaps during therapy and consequently was missed on the follow-up films.

Occasionally, there was an initial increase in the shadow rather than shrinkage. Under these circumstances, a diagnosis of pulmonary metastases rather than post-irradiation pneumonitis is likely to be made, and it is only when a succession of films demonstrates the inevitable shrinkage and even resolution that the true nature of the changes becomes evident.

A number of our cases have come to autopsy. Three in particular showed a typical sequence of roentgen findings, which were verified postmortem. In these instances there was no evidence of metastases. The problem of verification is complicated, however, by the fact that in so many of these cases pulmonary involvement develops terminally. Unless the pathologist is made aware of the possibility of post-irradiation changes prior to his dissection, he is likely to overlook these, particularly since, as in our series, they may not be extensive and tend to be concealed by the more massive neoplastic changes. In 1 such case a long sequence of films at our institution showed shrinkage and fibrosis in an upper lobe. The autopsy report from another hospital, however, approximately one month following our last

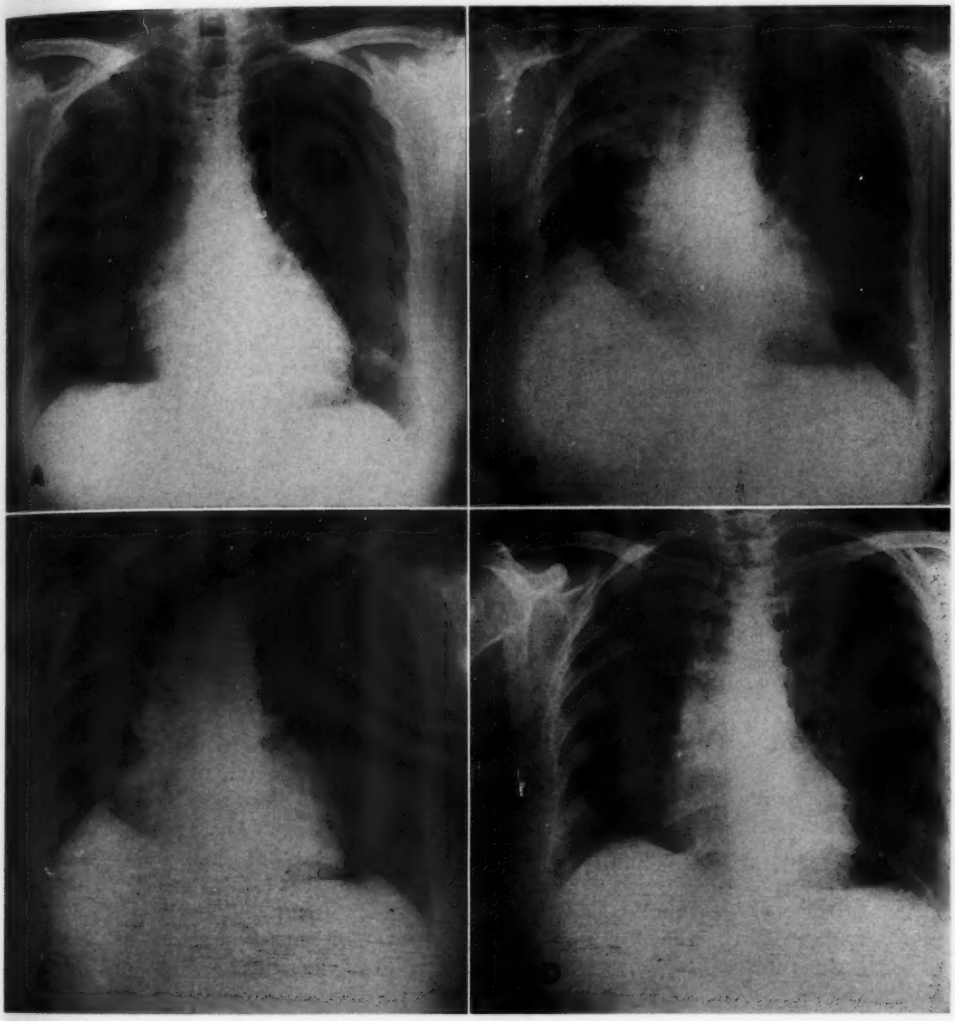


Fig. 4. A. Aug. 14, 1953. Normal chest prior to radiotherapy.
B. Jan. 22, 1954. Height of reaction. Patchy densities in right lung, widening of mediastinum, and tenting of diaphragm.
C. Feb. 26, 1954. Incomplete resolution.
D. Dec. 28, 1954. Resolution complete twelve months from appearance of changes.

film, described widespread metastases throughout the body, including both lungs, but failed to mention the small area of fibrosis, seen on the roentgenograms.

In 2 cases occurring early in our series, changes in the upper lobe were tentatively diagnosed as due to irradiation, although there was not available a suitably long sequence of chest films for a definite diagnosis. Both patients came to autopsy and were found to have pulmonary metastases in the areas under suspicion, which probably accounted for the x-ray shadows. No statement as to the presence of pulmonary fibrosis is found in the autopsy reports. The films of 1 of these patients showed fine linear strands leading from the right hilus to the right upper lobe (Fig. 5). In the other case, a complicated one, treated through the usual radiation fields,

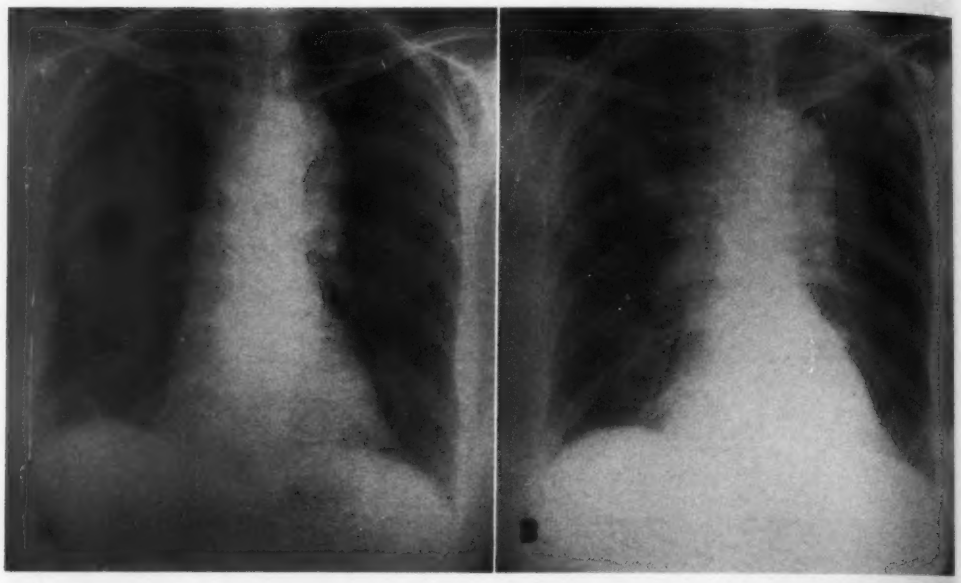


Fig. 5. A. Nov. 25, 1953. Normal chest prior to irradiation.
B. Oct. 8, 1954. Linear fibrotic strands leading from right hilus following irradiation, simulating characteristic radiation changes but actually representing metastatic disease.

but bilaterally, there were elevation of the hemidiaphragm and pleural effusion on one side. Failure of verification of the roentgen diagnosis in these 2 cases is not surprising. We would not now be so hasty in interpreting as post-irradiation pleuritis or fibrosis such non-specific changes.

In the majority of our cases with adequate sequences of films there was no problem in making a correct diagnosis. No difficulty was offered by changes localized to the lung under the area treated which were noted within six months following the end of radiotherapy and over a period of time did not consistently increase in size but remained constant or decreased and gradually resolved. Conversely, a lung shadow appearing outside the area treated, cannot very well be postirradiation pneumonitis. If the shadow, although within the area treated, continues to increase in size, it is probable that it represents a metastatic focus rather than fibrosis.

There are bound to be a few cases which, because of the extensiveness of the changes induced by irradiation, present a perplexing problem in diagnosis. One such case showed a right upper lobe density two months following the completion of radiotherapy. By the end of eight months there was roentgen evidence of a right pleural effusion (Fig. 6), but thoracentesis failed to reveal malignant cells in the fluid. At the time of this report the effusion was decreasing, being evidently the result of radiation to the pleura, as the patient has been well for a year and a half without treatment. A somewhat similar case (Fig. 7) was not included in our present series as radiotherapy was given through one field only, a 15 × 15-cm. portal taking in a recurrent internal mammary tumor. A tumor dose of 6,000 r was delivered in six weeks, and a pleural effusion subsequently developed on the irradiated side. The patient was treated at home, with numerous thoracenteses, and before long died. At autopsy she was found to be completely free of tumor. The major pathological findings were a large purulent pleural effusion and thickened pleura.

The roentgenograms reproduced in Figure 8 are those of a patient who showed,

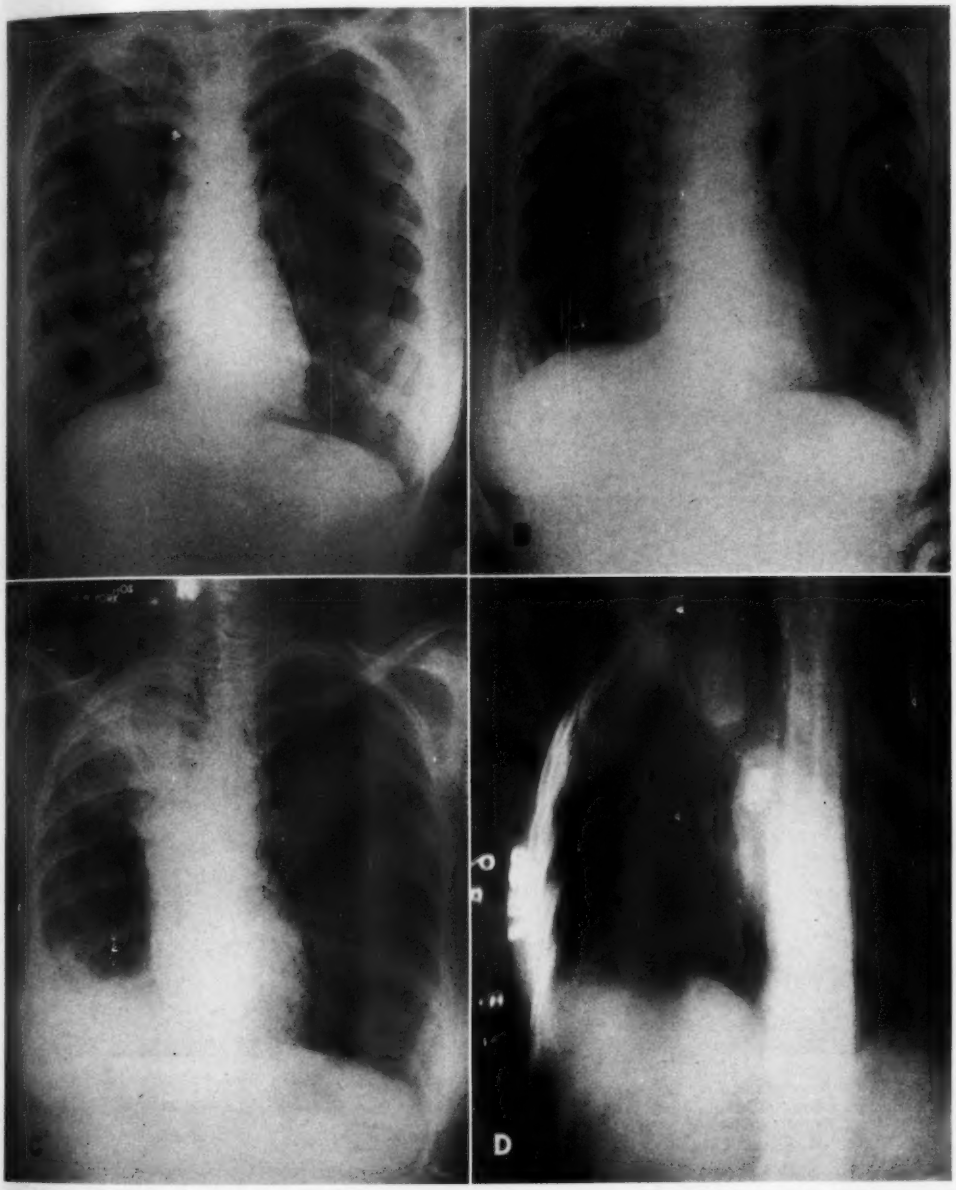


Fig. 6. A. Sept. 7, 1955. Normal chest prior to irradiation.
B. Dec. 20, 1955. Early changes; slight haze over upper lobe; elevation of right hilus; asymmetry of thorax, with small right lung and elevation of right diaphragm.
C. February 1956, six weeks later. Deviation of trachea to right; elevation of hilus and hemidiaphragm.
D. July 19, 1956. Tomogram showing findings unchanged. Shrinkage of upper lobe and deviation of trachea to the right.

first, typical pneumonitis with resolution and only minimal fibrotic changes. Films taken one year after completion of radiotherapy revealed the development of encapsulated left pleural fluid. The findings have remained the same for over more than a year, and at the time of this report the patient is doing well. We believe, there-

Fig. 7. A. Normal chest prior to irradiation.
B and C. June 27, 1955. Postero-anterior and lateral chest films showing well demarcated zone of fibrosis in region of middle lobe following atypical radiotherapy.
D. March 20, 1956. Lateral view showing extensive right pleural effusion.

fore, that we are justified in interpreting this finding as an effect of radiation upon the pleura.

One other case treated at the Frances Delafield Hospital is included in our series, although the chest examinations and surgical treatments were performed at another institution. This is perhaps the most interesting (and unfortunate) of our cases. The patient was treated through a 15 × 15-cm. left supraclavicular field and a 15 × 7-cm. left internal mammary field with a tumor dose of 5,400 r delivered to each of the areas over a period of forty-five days. Films taken within the next month were said to show a large pleural effusion and a density in the left upper lobe. Although at consultation the

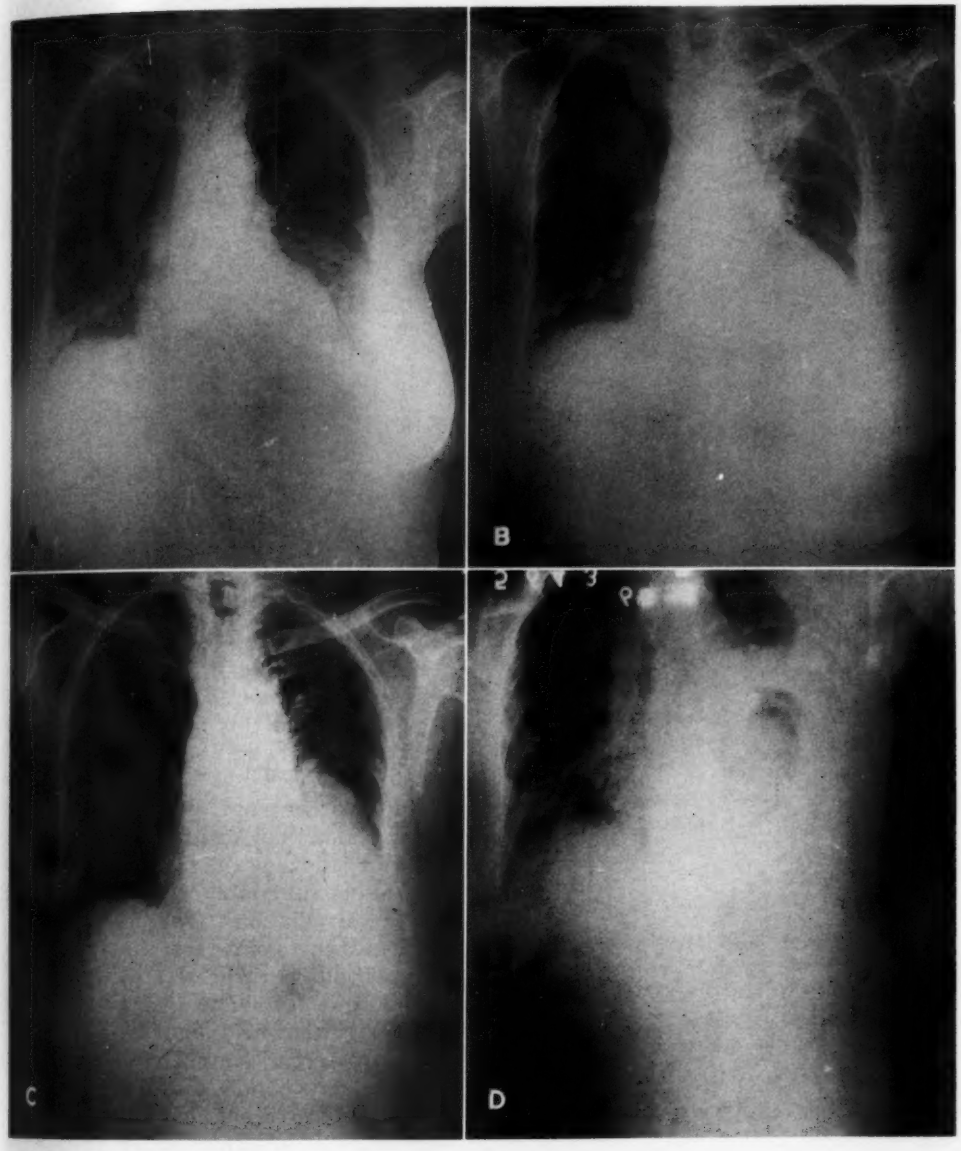


Fig. 8. A. May 12, 1955. Normal pretreatment film.
B. Aug. 18, 1955. Typical radiation pneumonitis on left.
C. June 5, 1956. Small fibrotic area in left upper lobe. Note bulging of left cardiac border.
D. June 5, 1956. Lateral recumbent view showing bulge due to pleural fluid. Cardiac silhouette normal.

opinion was expressed that these represented radiation changes and not metastases, it was the wish of the family that surgery be performed to remove this "metastatic" area. A lobectomy was performed, at which time the presence of the pleural effusion was confirmed. There were extensive radiation changes in the lung and no evidence of tumor. The pathological specimen showed in general the same changes as in an inflammation: edema, congestion, inflammatory cell infiltration, increased

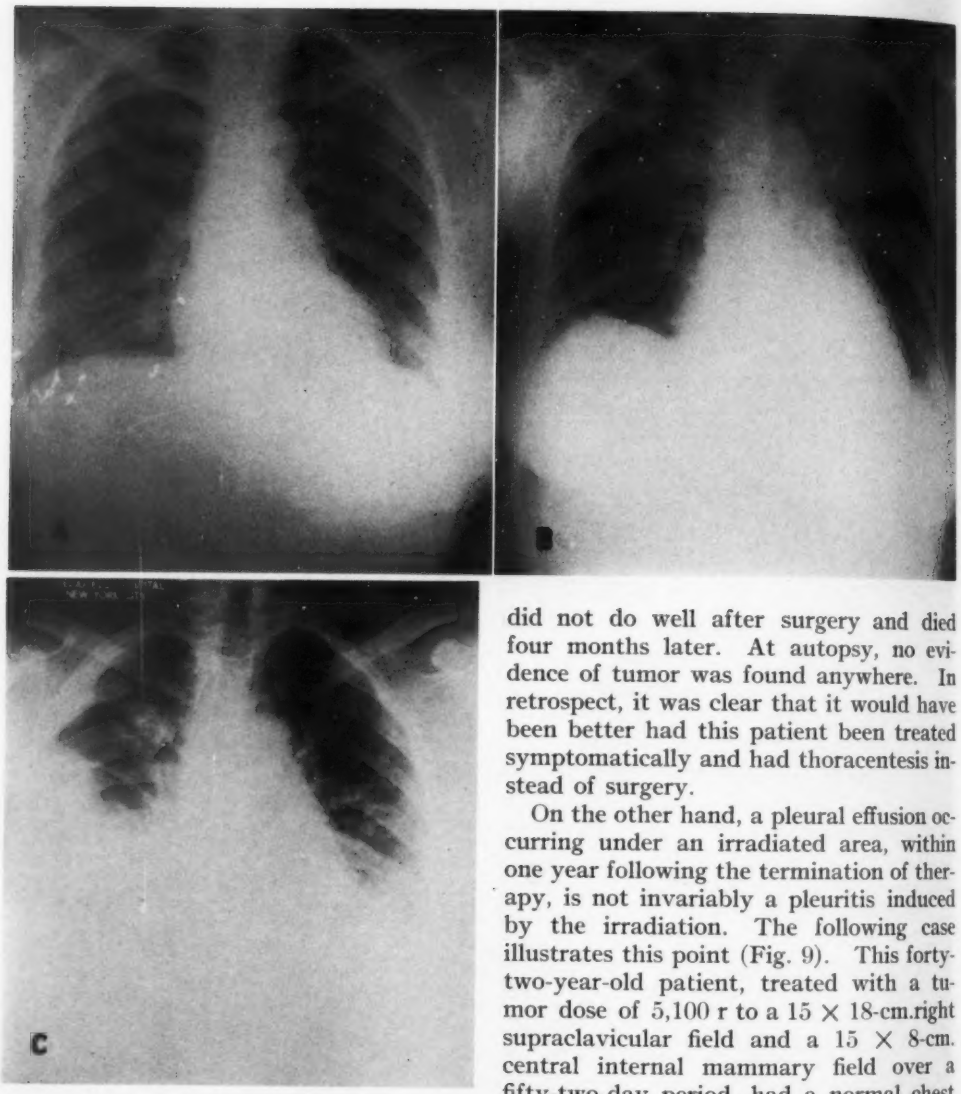


Fig. 9. A. June 13, 1955. Normal pretreatment film.
B. Jan. 27, 1956. Linear fibrotic strands leading from right hilus.
C. July 9, 1956. Residual changes in upper lobe; shrinkage indicated by elevated short fissure. Large right pleural effusion, proved by thoracentesis to be malignant.

number of thick elastic fibers scattered throughout the lung, and desquamation of the alveolar and bronchial epithelium followed by regeneration. The patient, who had always been in delicate cardiovascular balance, due to hyperthyroidism, did not do well after surgery and died four months later. At autopsy, no evidence of tumor was found anywhere. In retrospect, it was clear that it would have been better had this patient been treated symptomatically and had thoracentesis instead of surgery.

On the other hand, a pleural effusion occurring under an irradiated area, within one year following the termination of therapy, is not invariably a pleuritis induced by the irradiation. The following case illustrates this point (Fig. 9). This forty-two-year-old patient, treated with a tumor dose of 5,100 r to a 15 × 18-cm.right supraclavicular field and a 15 × 8-cm. central internal mammary field over a fifty-two-day period, had a normal chest film prior to treatment. Two months following the completion of therapy, a right upper lobe density was present. Three months after this, increasing lung fibrosis and an elevated right hemidiaphragm were observed. After another three months, the right lung changes remained the same, but densities in the left lung and pleura had appeared. They were thought to be metastatic. The next film, nine months following the end of radiotherapy, showed a right pleural effusion and,

again, left lung metastases. The nature of the fluid was determined by a right thoracentesis, which showed malignant cells.

The most successful management of subjective complaints associated with radiation fibrosis has been, in our experience, conservative symptomatic treatment: medication for cough, if at all possible without the addition of codeine; if dyspnea is present, rest or at least avoidance of strenuous exercise. In the very rare cases where cough and dyspnea cannot be controlled with these simple methods, we have used cortisone in daily dosages of 25 mg. for a maximum of three months and have seen gratifying subjective improvement.

If effusion persists and causes dyspnea, thoracentesis under strictly aseptic conditions is recommended. This will not only relieve dyspnea but may also prevent chronic thickening of the pleura and collapse of the lung. In doubtful cases it may permit the establishment of a diagnosis by cytologic studies.

Some authors having experience with much more pronounced unilateral fibrosis resulting from radiation, with symptoms not responding to any conservative management, have carried out pneumonectomies with good palliative results. In our opinion this should not be considered except in extreme cases.

It has been interesting to us to observe in this series a correlation between the dosage administered and any resulting roentgen signs and symptoms. There is a slight but definite increase in number and severity of changes with increasing dosage. Thirty patients were treated with dosages up to 5,000 r and 20 of these (66 per cent) have shown objective changes; 3 of the 20 had pleural effusion. Twenty patients received 5,000 r or more and, of these, 15 (75 per cent) have shown objective changes, with pleural effusions in 4. Subjective symptoms occurred only in the group receiving 5,000 r or more.

CONCLUSIONS AND SUMMARY

This study is based upon a group of 50 patients treated at the Francis Delafield Hospital (New York) for carcinoma of the breast. Radiotherapy was administered on the 2-million-volt unit through two anterior fields, one covering the internal mammary chain, the other, the supraclavicular and axillary areas. The tumor dose generally ranged from 3,000 to 5,000 r delivered to the level of the lymph nodes in three to five weeks.

Thirty-five patients showed roentgenographic evidence of post-irradiation changes in the lung while 5 patients had roentgenographic lung findings proved to be due to metastatic tumor. Most of the post-irradiation changes were minimal, consisting of pneumonitis followed by shrinkage of the lung and fibrosis. These changes were reversible in some cases.

Only 7 patients had subjective respiratory complaints which could be attributed to radiation. These were chiefly a dry cough or dyspnea, which either did not persist or else responded to conservative treatment. In the cases where pleural effusion was present, thoracentesis was employed under strictly aseptic conditions.

There was a slight but definite increase in changes with increasing tumor dose. As might be expected, patients manifesting pleural effusion comprised the highest percentage of those having subjective symptoms.

An attempt has been made to emphasize the importance of recognizing pneumonitis, fibrosis and the less common pleural effusion following irradiation of breast carcinoma. The difficulty in arriving at a correct diagnosis without an adequate sequence of chest roentgenograms has been stressed. A correct interpretation of the roentgenologic findings may make the difference between proper conservative management of symptoms so induced and harmful further irradiation or ill-advised surgery.

REFERENCES

BERGMANN, M., AND GRAHAM, E. A.: Pneumonectomy for Severe Irradiation Damage of the Lung. J. Thoracic Surg. **22**: 549–567, December 1951.

CHU, F. C. H., PHILLIPS, R., NICKSON, J. J., AND MCPHEE, J. G.: Pneumonitis Following Radiation

Therapy of Cancer of the Breast by Tangential Technic. Radiology **64**: 642–653, May 1955.

DAVIS, K. S.: Intrathoracic Changes Following X-Ray Treatment: A Clinical and Experimental Study. Radiology **3**: 301–322, October 1924.

DESJARDINS, A. U.: Action of Roentgen Rays and Radium on the Heart and Lungs. Am. J. Roentgenol. **28**: 701–720, November 1932.

DESJARDINS, A. U.: Reaction of the Pleura and Lungs to Roentgen Rays. Am. J. Roentgenol. **16**: 444-448, November 1926.

DOWNS, E. E.: Lung Changes Subsequent to Irradiation in Cancer of the Breast. Am. J. Roentgenol. **36**: 61–64, July 1936.

ENGELSTAD, R. B.: Pulmonary Lesions after Roentgen and Radium Irradiation. Am. J. Roentgenol. **43**: 676–681, May 1940.

EVANS, W. A., AND LEUCUTIA, T.: Intrathoracic Changes Induced by Heavy Radiation. Am. J. Roentgenol. **13**: 203–220, March 1925.

FIKE, R. H.: The Occurrence of Roentgen Pleuropneumonitis in Treatment of Breast Cancer. Am. J. Roentgenol. **27**: 509–512, April 1932.

FREID, J. R., AND GOLDBERG, H.: Post-Irradiation Changes in the Lungs and Thorax. A Clinical, Roentgenological and Pathological Study, with Emphasis on the Late and Terminal Stages. Am. J. Roentgenol. **43**: 877–895, June 1940.

GROOVER, T. A., CHRISTIE, A. C., AND MERRITT, E. A.: Intrathoracic Changes Following Roentgen Treatment of Breast Carcinoma. Am. J. Roentgenol. **10**: 471–476, June 1923.

GROOVER, T. A., CHRISTIE, A. C., AND MERRITT, E. A.: Roentgen Pleuropneumonitis. South. M. J. **20**: 153–158, February 1927.

GUTTMANN, R. J.: The Treatment of Inoperable Carcinoma of the Breast with Conventional 250-kv Irradiation as Compared with 2-mv Irradiation. Radiology **67**: 497–506, October 1956.

HARRIS, J. H., JR., TUDDENHAM, W. J., STANTON, L., GLAUSER, F., AND PENDERGRASS, E. P.: The Development of a Chest Phantom for Use in Radiologic Dosimetry. Radiology **67**: 805–813, December 1956.

HINES, L. E.: Fibrosis of Lung Following X-Ray Treatments for Tumor. J.A.M.A. **79**: 720–722, Aug. 26, 1922.

HOLFELDER, H.: Ist die postoperative Bestrahlung beim Mammakarzinom berechtigt? Strahlentherapie **22**: 667–688, 1926.

HSIEH, C. K., AND KIMM, H. T.: Changes in the Lungs and Pleura Following Irradiation of Extrathoracic Tumors. Am. J. Roentgenol. **37**: 802–810, June 1937.

JACOBSON, L. F., AND KNAUER, I. S.: Correction Factors for Tumor Dose in the Chest Cavity Due to Diminished Absorption and Scatter in Lung Tissue. Radiology **67**: 863–876, December 1956.

JACOBSEN, V. C.: The Deleterious Effects of Deep Roentgen Irradiation on Lung Structure and Function. Am. J. Roentgenol. **44**: 235–248, August 1940.

KAPLAN, I. I., AND BELL, D.: Pleuropulmonitis Following Irradiation. Am. J. Roentgenol. **39**: 387–392, March 1938.

LEACH, J. E., FARROW, J. H., FOOTE, F. W., JR., AND WAWRO, N. W.: Fibrosis of the Lung Following Roentgen Irradiation for Cancer of the Breast. A Clinical Study. Am. J. Roentgenol. **47**: 740–747, May 1942.

LEACH, J. E.: Abnormal Pulmonary Physiology as a Result of Chronic Irradiation Pleuropulmonitis. A Preliminary Report. Am. J. Roentgenol. **50**: 772–778, December 1943.

MCINTOSH, H. C., AND SPITZ, S.: A Study of Radiation Pneumonitis. Am. J. Roentgenol. **41**: 605–615, April 1939.

MCINTOSH, H. C.: Changes in the Lungs and Pleura Following Roentgen Treatment of Cancer of the Breast by Prolonged Fractional Method. Radiology **23**: 558–566, November 1954.

MAY, E. A.: Methods of Roentgen Treatment in Carcinoma of the Breast. Report of 210 Cases. Radiology **21**: 420–431, November 1933.

MEURK, M. L., AND CHU, F. C. H.: Physical Aspects of the Tangential Technic in Roentgen Therapy of Cancer of the Breast. Unpublished.

TYLER, A. F., AND BLACKMAN, J. R.: Effect of Heavy Radiation on the Pleurae and Lungs. J. Radiol. **3**: 469–475, November 1922.

WARREN, S., AND GATES, O.: Radiation Pneumonitis. Experimental and Pathological Observations. Arch. Path. **30**: 440–460, July 1940.

WARREN, S., AND SPENCER, J.: Radiation Reaction in the Lung. Am. J. Roentgenol. **43**: 682–701, May 1940.

WEATHERWAX, J. L., AND ROBB, C.: Determination of Radiation Values in Lung Tissue with Variable Qualities of Radiation. Radiology **14**: 401–409, April 1930.

WIDMANN, B. P.: Irradiation Pulmonary Fibrosis. Am. J. Roentgenol. **47**: 24–38, January 1942.

WINTZ, H.: Injuries from Roentgen Rays in Deep Therapy. Am. J. Roentgenol. **10**: 140–147, February 1923.

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SUMMARIO IN INTERLINGUA

Alterationes in Pulmon e Pleura Post Therapia a Duo Megavolt Pro Carcinoma Mammari

Un studio del alterationes post-irradiational in pulmones e pleura esseva effectuate in 50 patientes tractate pro cancere mammari per medio del apparatura a duo megavolt al Hospital Francis Delafield in New York. Le tractamento esseva administrate via duo campos. Le prime coperiva le interne catena mammari de nodos lymphatic, le secunde le areas supraclavicular e axillari. Le dosage al tumor variava in general ab 3.000 a 5.000 r al nivello del nodos lymphatic e esseva administrate in inter tres e cinque septimanas.

Trenta-cinque patientes exhibiva alterationes resultante del irradiation. In 5, cancere metastatic esseva demonstrate. Le majoritate del alterationes irradiational esseva minor, consistente de pneumonitis sequite per contraction del pulmon con

fibrosis. Effusion pleural esseva presente in alicun casos. Resolution del alterationes esseva un occurrentia frequente.

Le severitate del alterationes esseva apparentemente relationate al dosage. Le patientes qui recipeva le plus grande quantitates de radiation monstrava levemente plus intense reactiones.

Il es importantissime distinguer le pneumonitis, fibrosis, e le minus frequente effusion pleural que occurre como resultato del irradiation ab le alterationes que es le effecto de un tumor metastatic. Pro iste objectivo, un adequate serie de roentgenogrammas thoracic es indispensabile. Le interpretation correcte del constationes roentgenographic va resultar in le appropriate tractamento conservative de symptomas e preveni nocive irradiation additional o mal-concipite intervention chirurgic.

The Use of Oral Antihistamines in Intravenous Urography[1]

HAROLD L. ATKINS, M.D.,[2] and PHILIP J. HODES, M.D.

ROENTGENOLOGIC exploration of the urinary tract is performed routinely as a diagnostic procedure. Unfortunately, however, the administration of contrast materials in intravenous urography is frequently attended by untoward reactions and may even result in death (14–16). There is a continuing search for the ideal contrast agent which will provide adequate visualization of the urinary tract without producing undesirable side-effects.

Various mechanisms are responsible for the production of side-reactions to the opaque media. The more serious complications are probably due to drug idiosyncrasy or anaphylaxis. Other effects may result from pharmacological properties of these compounds.

The use of oral antihistaminics in combating the serious secondary effects of contrast materials has been proposed and the intention of studying their effects at this institutiton has been stated (15). There is conflicting evidence concerning the efficacy of antihistaminic premedication in reducing the severity or eliminating the side-reactions to intravenous contrast agents. With this in mind, the following study, the first of a two-part project, was carried out.

METHOD

This study includes all patients undergoing intravenous urography over a one-year period at the Radiologic Clinic of the Hospital of the University of Pennsylvania. Ward, private, and out-patients are included. The out-patient group received no premedication. The total number of urographic examinations was 1,580, after exclusion of 183 because of insufficient data or the use of contrast agents other than 50 per cent Neo-Iopax, the standard material used in this department at the time of the study. Where a patient had more than one examination, each is included as a separate study.

All patients were prepared for excretory urography in the usual manner. Food and fluids were withheld following the evening meal of the day prior to examination. A mild laxative was administered that evening.

The patients were divided into eight groups according to the antihistamine premedication received. This number included two control groups, one of which had no premedication while the other was given placebos. Code numbers were assigned to the envelopes containing the preparation to be used so that personnel on the hospital floors as well as in the Department of Radiology were unaware of the actual medication in any case.

The groups were as follows, the figures in parentheses representing the strength of each tablet.

1. No antihistamine
2. Placebo
3. Pyribenzamine (50 mg.)
4. Thenfadil (15 mg.)
5. Chlortrimeton (4 mg.)
6. Benadryl (50 mg.)
7. Thephorin (25 mg.)
8. Clistin Maleate (4 mg.)

One tablet was given the evening before and another one hour prior to the examination.

All patients had a complete allergic history taken on a standard form which has been previously described (14). A test dose of 0.1 c.c. of 50 per cent Neo-Iopax was given intradermally ten minutes prior to examination and the results were recorded. Various members of the department took the histories and performed the

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TABLE I: INCIDENCE OF REACTIONS TO UROGRAPHIC MEDIUM (50 PER CENT NEO-IOPAX) WITH AND WITHOUT ORAL ADMINISTRATION OF VARIOUS ANTIHISTAMINES

Antihistamine Tablet Size in Parentheses	No. Patients	Nausea and Vomiting	Flush	Venospasm	Asthma and Urticaria	Syncope
None	493	65(13.2%)	146(29.6%)	42 (8.5%)	4(0.8%)	22(4.4%)
Placebo	66	8(12.1%)	27(40.9%)	8(12.1%)	0	3(4.6%)
Pyribenzamine (50 mg.)	139	20(14.4%)	44(31.6%)	17(12.2%)	2(1.4%)	5(3.6%)
Thenfadil (15 mg.)	94	15(16.0%)	9 (9.6%)	3 (3.2%)	0	1(1.1%)
Chlortrimeton (4 mg.)	158	25(15.8%)	53(33.5%)	24(15.2%)	1(0.6%)	7(4.4%)
Benadryl (50 mg.)	36	3 (8.3%)	16(44.5%)	6(16.7%)	1(3.2%)	3(8.3%)
Thephorin (25 mg.)	10	2(20.0%)	3(30.0%)	0	0	1(10.0%)
Clistin Maleate (4 mg.)	584	58(9.9%)	155(26.6%)	44 (7.5%)	0	13(2.2%)
TOTAL	1580	196	453	144	8	55
X^2		8.00	30.41	18.77		
P		≥ 0.03	≥ 0.001	≥ 0.01		

skin tests and contrast injections. Twenty or 30 c.c. of 50 per cent Neo-Iopax (according to the patient's weight) was injected rapidly (10–15 seconds) into an antecubital vein and all immediate reactions were observed by the physician who had performed the injection. The patients were observed for reactions throughout their stay in the Department of Radiology (usually more than forty minutes). Delayed reactions were reported to the department and recorded on the standard form.

RESULTS

In summarizing the results of this study no attempt was made to analyze separately those cases with an allergic history. Nor were reactions graded as to severity. It was felt that the range of variation is so great as to preclude objective evaluation. No fatalities were encountered, and the incidence of acute allergic or anaphylactic phenomena was very low.

The results are given in Table I, which shows for each group the number experiencing reactions under the major categories, namely nausea and vomiting, flushing, venospasm, asthma and urticaria, syncope and shock.

An analysis of the results was carried out according to the "chi-square" method. The assumption in performing the computation was that no beneficial effects were derived from the use of antihistamines under the conditions of this study. For each category of reaction the probability, P, that the results could be duplicated by chance was computed. If P was greater than 0.05 it was assumed that no significant difference was obtained with the use of antihistamines; *i.e.*, the results could have been duplicated by chance alone in one instance out of twenty or better.

Nausea and Vomiting: This reaction varied from mild nausea to rather severe retching. The frequency of occurrence in the controls (13.2 per cent) is in agreement with most other reports. No significant variation from the control group was found in those receiving the various antihistamines (P greater than 0.03).

Flushing was considered to have occurred only when an actual erythema of the face developed. A mere "feeling of warmth" was not included as a positive reaction. Analysis would seem to indicate that the reduction in the number of patients with this reaction from the control of 29.6 per cent to 9.6 per cent in the Thenfadil group is significant (P less than 0.001). A flush, however, is somewhat difficult to evaluate objectively. Negroes constituted a considerable percentage of our patients and there were others who had naturally florid complexions. The problem of evaluation is reflected in the great variability of results, particularly in the apparent increase in reactions in patients given placebos. In any event, one would not expect antihistamines to exert an influence in the frequency of this reaction.

Venospasm was manifest by severe pain in the arm or shoulder along the course of the vein used for injection.

TABLE II: SUMMARY OF REACTIONS OBSERVED WITH AND WITHOUT ANTIHISTAMINES

	Number	Nausea and Vomiting	Flush	Venospasm	Asthma and Urticaria	Syncope
No antihistamine	559	73(13.0%)	173(30.9%)	50(8.9%)	4(0.7%)	25(4.5%)
All antihistamines	1021	123(12.0%)	280(27.4%)	94(9.2%)	4(0.4%)	30(2.9%)
TOTAL	1580	196	453	144	8	55
X^2		0.29	2.19	0.03	0.80	2.57
P		≥ 0.5	≥ 0.1	≥ 0.8	≥ 0.3	≥ 0.1

Again, one would not expect any differences due to the administration of antihistamines. Significant variations were encountered in this category (P less than 0.01). The reaction seemed to be favorably affected by Clistin Maleate but was adversely affected to an even greater degree by Benadryl. The explanation for this is unknown. Certainly the amount of venospasm is dependent to a large degree on the rapidity with which the material is injected.

Asthma and Urticaria: This category includes acute allergic phenomena such as hives, pruritus, sneezing, and bronchospasm. A very low incidence of such reactions was found, the number being too low to allow a statistical analysis by the "chi-square" method. The antihistamines appeared to have no demonstrable effect in reducing the number of reactions.

Syncope: Patients complained of feeling "dizzy," "strange," or "about to faint," although none lost consciousness or displayed a shock-like state. This type of reaction, in addition to drug sensitivity, is probably often secondary to psychogenic factors or even lack of food when the examination is performed after prolonged fasting. Again the incidence was too low to permit analysis by the "chi-square" method. No major variations in results were observed secondary to the antihistamines.

Deaths: No fatalities occurred.

Summary: An overall evaluation of the results shows no consistent action of antihistamines in general in reduction of annoying side-effects of intravenous urographic contrast agents (Table II). It is noted, however that Clistin Maleate consistently showed an effect (Table I). There were fewer reactions in all categories in the patients receiving this premedication. It is statistically significant that this should occur in five out of five categories but the differences are small and would not warrant use of the drug routinely.

DISCUSSION

The manifestation of intolerance to the usual urographic contrast media is of several types and indicates more than one underlying mechanism. The various substances used produce reactions of the same type but differing in severity and frequency. Reactions may be classified as due to the pharmacologic properties of the drugs (9, 18) or to true allergy and idiosyncrasy (16).

The effects on the cardiovascular system are prominent and are attributable to the pharmacologic properties of the contrast agents. Initial constriction of vessels may occur, followed shortly by dilatation. The initial constriction is more pronounced with Diodrast than with Neo-Iopax and with rapid rather than slow injection. A rapid injection may cause a lowering of the systemic blood pressure, whereas a slow injection will have no effect (18). Neo-Iopax may depress the action of the heart and reduce cardiac output. This effect, in turn, may be reversed by another property of the drug, coronary artery dilatation (18).

Syncope, nausea, and vomiting may be due to a vagal action (9) or to allergic properties of the contrast medium. Other, obviously anaphylactic reactions may occur, such as sneezing, asthma, urticaria,

and convulsions (13, 9, 10, 16). Various tests to determine prior hypersensitivity have been devised in order to prevent knowingly exposing a patient to an allergen (1, 2, 12). These are often ineffective. An allergic state can exist in the absence of positive skin or intraocular tests. The majority opinion at this time seems to be that sensitivity tests are of no value in predicting reactions to contrast media (11).

Reactions to the urographic agents have also been attributed to impurities such as pyrogens and free iodine (16).

In an attempt to escape the deleterious effects of contrast materials, various new media have been tried. Not one has been found to be entirely free of noxious properties. Allergic and other reactions have occurred to all of them. Inman (9) has tried intravenous administration of phenobarbital and atropine in the belief that nausea and vomiting may be due to vagal stimulation or an autonomic imbalance. His results indicated that atropine might be helpful but that phenobarbital was ineffective in lessening the incidence of reactions.

The antiallergic properties of antihistamines are well known. They act as blocking agents against histamine, an important factor in the allergic state. In addition, they possess antiemetic and parasympatholytic (atropine-like) properties (8). It is logical to consider their use in combating the side-effects of contrast materials. It is to be expected that they would be useful in reducing the incidence of nausea and vomiting as well as allergic phenomena. Their sedative action would also seem desirable in this connection. It would not be expected that these drugs be effective against primarily pharmacologic properties such as flush and venospasm.

Several studies have been published relating the use of orally administered antihistamines in intravenous urography with conflicting conclusions regarding their efficacy (4, 5, 6, 11). Getzoff, on the basis of a small group of patients, believed that 50 to 200 mg. of Pyribenzamine orally, prior to injection of the contrast material, reduced the number of general reactions (5, 6). Crepea, Allanson and DeLambre (4) concluded that Pyribenzamine and Trimeton were ineffective in this capacity. Our observations support this latter view. The routine use of oral antihistamines in intravenous urography to control side-reactions does not appear to us to be warranted. This is particularly so when one considers the extremely low incidence of the purely allergic phenomena, against which the antihistamines would be expected to be more effective.

The administration of an antihistamine intravenously simultaneously with the contrast material has been reported on more favorably (10, 13, 17). Several authors have been impressed by a marked reduction in the incidence of nausea and vomiting, as well as other types of reactions. This experience however, has not been universal (3, 7, 16).

It may be that the blood concentration of antihistamine at the time of injection of the contrast agent is most important. A study of the use of intravenous antihistamine injected simultaneously with the opaque material will be the subject of another report from this institution.

SUMMARY

A series of 1,580 urographic examinations was studied with regard to the effect of antihistamines in reducing the number of side-reactions when administered orally prior to the examination.

Statistically significant variations were noted in the "flush" and "venospasm" response following certain antihistamines, a finding which was not expected and may be accounted for by several factors.

It is concluded that the routine use of oral antihistamines in intravenous urography is not warranted.

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REFERENCES

1. ALYEA, E. P., AND HAINES, C. E.: Intradermal Test for Sensitivity to Iodopyracet Injection, or "Diodrast." J.A.M.A. **135**: 25–27, Sept. 6, 1947.
2. ARCHER, V. W., AND HARRIS, I. D.: An Ocular Test for Sensitivity to Diodrast Prior to Intravenous Urography. Am. J. Roentgenol. **48**: 763–765, December 1942.
3. BERSACK, S. R., AND WHITAKER, T. E., JR.: Effect of Diphenhydramine (Benadryl) on Side-Reactions in Intravenous Urography. Arch. Int. Med. **91**: 618–625, May 1953.
4. CREPEA, S. B., ALLANSON, J. C., AND DELAMBRE, L.: The Failure of Antihistaminic Drugs to Inhibit Diodrast Reactions. New York State J. Med. **49**: 2553–2558, Nov. 1, 1949.
5. GETZOFF, P. L.: Use of Antihistamine Drug Prophylaxis against Diodrast Reactions. J. Urol. **65**: 1139–1142, June 1951.
6. GETZOFF, P. L.: The Use of an Histamine Antagonist in Intravenous Pyelography. New Orleans M. & S. J. **101**: 22–25, July 1948.
7. GILG, E.: The Influence of Diphenhydramine (Benadryl) on the Side-Effects of Diodone in Urography. Acta radiol. **39**: 299–307, April 1953.
8. GOODMAN, L. S., AND GILMAN, A.: The Pharmacological Basis of Pharmacology, Toxicology, and Therapeutics for Physicians and Medical Students. New York, The Macmillan Co., 2nd ed., 1955.
9. INMAN, G. K. E.: A Comparison of Urographic Contrast Media, with Particular Reference to the Aetiology and Prevention of Certain Side Effects. Brit. J. Radiol. **25**: 625–631, December 1952.
10. MOORE, T. D., AND SANDERS, N.: Reaction to Urographic Agents With and Without Antihistamines. J. Urol. **70**: 538–544, September 1953.
11. MULLEN, W. H., JR., AND HUGHES, C. R.: Intravenous Urographic Contrast Media. Controlled Study of Diodrast and Neo-Iopax. Am. J. Roentgenol. **68**: 903–914, December 1952.
12. NATERMAN, H. L., AND ROBINS, S. A.: Cutaneous Test with Diodrast to Predict Allergic Systemic Reactions from Diodrast Given Intravenously. J.A.M.A. **119**: 491–493, June 6, 1942.
13. OLSSON, O.: Antihistaminic Drugs for Inhibiting Untoward Reactions to Injections of Contrast Medium. Acta radiol. **35**: 65–70, January 1951.
14. PENDERGRASS, E. P., CHAMBERLIN, G. W., GODFREY, E. W., AND BURDICK, E. D.: A Survey of Deaths and Unfavorable Sequelae Following Administration of Contrast Media. Am. J. Roentgenol. **48**: 741–762, December 1942.
15. PENDERGRASS, E. P., HODES, P. J., TONDREAU, R. L., POWELL, C. C., AND BURDICK, E. D.: Further Considerations of Death and Unfavorable Sequelae Following the Administration of Contrast Media in Urography in the United States. Acta radiol. Suppl. 116, 1954.
16. SANDSTRÖM, C.: Contrast Media for the Kidneys, Heart and Vessels, and Their Toxicity. Acta radiol. **39**: 281–298, April 1953.
17. SIMON, S. W., BERMAN, H. I., AND BARALD, F. C.: Prevention of Reactions in Intravenous Urography. Ohio State M. J. **50**: 247–248, March 1954.
18. WEATHERALL, M.: Pharmacological Actions of Some Contrast Media and Comparison of Their Merits. Brit. J. Radiol. **15**: 129–137, May 1942.

SUMMARIO IN INTERLINGUA

Le Uso de Antihistaminas Oral in Urographia Intravenose

Un serie de 1.580 examines urographic con 50 pro cento de Neo-Iopax esseva studiate con respecto al effecto de antihistaminas super le reactiones lateral que esseva evocate per le medio. Sex differente antihistaminas esseva usate. Illos esseva administrate per via oral ante le examine urographic. Un de duo gruppos de controlo remaneva sin tractamento, durante que le secunde recipeva un medication fictitie.

Es exprimite le opinion que le uso routinari de antihistaminas in le practica urographic es non justificate. Un evalutation general del resultatos per medios de analyse statistic demonstrava nulle action regular del antihistaminas in effectuar un reduction del reactiones lateral al agente de contrasto. Variationes de genere statisticamente significative esseva notate in le occurrentia de rubor e de venospasmos post certes del drogas usate. Tamen, on non pote supponer que iste reactiones responde al therapia a antihistaminas, e le reduction de lor incidentia pote esser attribuite a altere factores.

A Bronchographic Sign of Chronic Bronchitis[1]

LIEUT. BILLY P. SAMMONS, (MC) USN, LIEUT. WILLIAM O. PISCHNOTTE, (MC) USN, and LIEUT. JOHN R. WILLIAMS, (MC) USN

THE DIAGNOSIS of bronchitis by the radiologist is usually based on the observation of increased irregular parenchymatous markings and emphysematous changes. This evaluation is essentially an impression founded on experience closely correlated with many long-term histories. We are presenting here an objective sign, apparently pathognomonic of bronchitis, which we believe will be of help in this difficult diagnostic problem. It consists in the bronchographic demonstration of the dilated mucous gland ducts lining the major bronchi.

Though Sicard and Forestier (10) originated the present bronchographic technic in 1922, it remained for Morlock and Pinchin (6), in 1933, to report some of the bronchographic findings in chronic bronchitis. They described sacculations between the cartilaginous rings, most marked in the trachea, and "roundish patches of Lipiodol which appeared to be outside the bronchial tree." The significance of glandular involvement of the bronchial mucosa was first described by Stutz (13) and soon thereafter beautifully illustrated in 2 cases reported by Stiller (12) in 1949. Fischer (2), in 1950, reported 5 additional cases, attributing his success to the use of a water-soluble medium. More recently Simon (11) and Gudbjerg (3) have reported other cases. The latter author demonstrated the glandular findings with oily contrast material. He felt that the low reported incidence of glandular involvement was due to a lack of appreciation of the significance of such changes rather than to the type of medium used. Simon in reviewing the bronchograms of a large number of bronchitic patients found glandular involvement in 50 per cent.

CLINICO-PATHOLOGICAL ASPECTS

The clinical diagnosis of chronic bronchitis is essentially one of exclusion (5). The possibility can be seriously entertained after elimination of such entities as asthma, bronchiectasis, upper respiratory tract infectious foci, pulmonary abscesses, cystic disease, tuberculosis, pneumoconioses, left ventricular failure, aortic aneurysm, and carcinoma. The symptoms are cough, sputum, and dyspnea, and the condition is most commonly found in middle-aged males with a fairly strong family history (7).

The pathophysiology of bronchitis can best be understood by a consideration of the effects of irritation on the bronchial mucosa. In response to a variety of noxious agents there is an increased production of mucus. This excess mucus was microscopically demonstrated by Reid (8, 9) to be due to a hypertrophy of the mucus-secreting elements. Large numbers of goblet cells were also noted in the bronchioles, where they are normally scarce. Other early microscopic findings are dilatation of the mucous gland ducts (this being responsible for the bronchographic findings described below), edema, and round-cell infiltration of the physiologically weakened bronchial wall.

In advanced cases the above findings occur in addition to localized and diffuse dilatation of the bronchioles, obliteration of the lumen, purulent bronchitis, small foci of parenchymal consolidation, and abscesses. One author (1) reported polypoid thickening with areas of squamous metaplasia. Alveolar changes, consisting of emphysema, collapse, pneumonia, and mucous plugs all lend support to the hypothesis that the irritation results in excess mucus and breakdown of glands and epithelium by

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The opinions expressed are those of the authors and are not to be construed as official or representing the views of the Navy Medical Department.

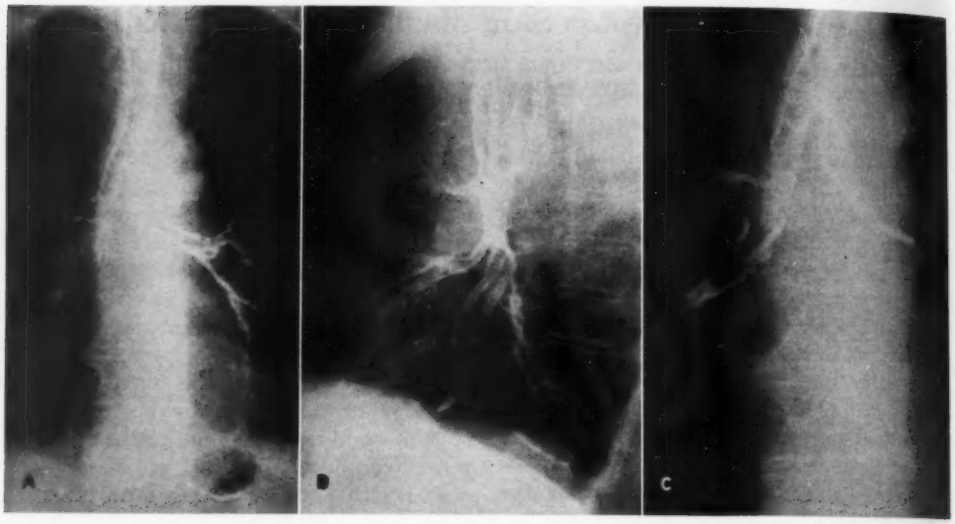

Fig. 1. Case I. A. Bronchogram demonstrating the numerous contrast-filled bronchial glands of the main stem and lobar bronchi.
B. Lateral projection showing the above changes, as well as distortion of the bronchi with alternating areas of dilatation and constriction.
C. Marked involvement of the bronchial glands of the right upper lobe bronchus.

suppurative processes. The involvement of the alveoli is probably due to the endobronchial spread of the bacteria-laden mucus. This is confirmed by the finding of mucus, not normally present, in histologic sections of the alveoli.

ROENTGEN FINDINGS

Routine roentgenograms in various projections and phases of respiration augmented by fluoroscopic methods are of relatively little help in the diagnosis of bronchitis. This is because of the necessity for placing reliance on the non-specific and difficult evaluation of minimal emphysema and increased bronchovascular markings. The bronchogram, on the other hand, not only helps exclude other disease processes, but is capable in a large percentage of cases of revealing the effects of the irritative process by filling of the dilated ducts of the mucous glands. It is the latter that act as cesspools for stagnant secretions and allow the secondary infection to bore deeper into the wall, destroying more and more tissue. These intramural dilated ducts probably should not be spoken of as diverticula. The latter term should be reserved for the shallow concavities noted between the cartilaginous rings resulting from high cough pressures against the weakened muscle. Simon (11) believes that in cases of bronchiectasis which demonstrate diffuse areas of ductal involvement coincident bronchitis should be reported.

We feel it is important to realize that in the dyspneic patient only 5 to 8 c.c. of contrast material is needed for the demonstration of these ducts, since the major involvement is in the main stem and lobar bronchi.

CASE REPORTS

CASE I: C. B. D., a 72-year-old white male, was admitted on Nov. 9, 1956, with an eighteen-month history of cough productive of yellow-green sputum, non-odorous, and worse in the morning. Dyspnea, low-grade fever and a 15-pound weight loss were also present. The patient had smoked one pack of cigarettes daily for many years.

The family history was of interest in that the mother and one sister had died of influenza, and another sister of pneumonia. The patient had had malaria in 1910 and 1933, typhoid in 1910, and pneumonia in 1918 and 1947. He was on maintenance doses of digitalis for arteriosclerotic heart disease. An allergy to ragweed was also noted. Physical examination revealed coarse rhonchi at both lung bases, clearing with cough on the left, and a 2-plus benign prostatic hypertrophy.

In the hospital, the patient was treated with expectorants, and a course of chloramphenicol and penicillin, as well as continued digitalis. His temperature originally rose to as high as 102° F. but gradually returned to normal.

Bronchoscopy revealed excessive loose mucous secretions. Papanicolaou smears were negative. A PPD number 1 skin test was positive; a complete blood count and urine examinations were normal; the Kahn test was negative, as were cultures for acid-fast bacilli. The electrocardiogram revealed notched P waves but was otherwise negative. Sputum cultures showed non-hemolytic *Staphylococcus aureus* and alpha streptococci. Chest films revealed blunting of the right costophrenic angle and diffuse interstitial fibrosis bilaterally. The bronchographic findings are shown in Figure 1.

The patient was discharged improved on Dec. 8, 1956, on digitalis and oral antibiotics, to be followed as an out-patient.

CASE II: G.H., a 20-year-old white male, was first admitted on May 28, 1956, with a three-month history of cough productive of sputum, occasionally blood-streaked, and weight loss. Skin tests with PPD, coccidioidin, and histoplasmin were negative; an old tuberculin test was questionably positive. Cultures for acid-fast bacilli were negative. Bronchoscopic findings were normal. X-rays revealed a consolidation of the lingula which cleared with oxytetracycline therapy, and the patient was discharged on July 17, 1956.

He was readmitted on Aug. 21, 1956, with continued complaint of cough, worse in the morning and productive of a cupful of yellow-green sputum, occasionally blood-tinged, per day. He had lost 15 pounds in five weeks despite a good appetite, was easily fatigued, and had left anterior chest pain on exertion.

The past history was non-contributory except for frequent upper respiratory infections. A sister had arrested tuberculosis since 1947. Physical examination was essentially negative.

In the hospital, symptoms continued, despite antibiotics and expectorants, with a low-grade fever rising as high as 99.8° F. Intravenous pyelography, ear, nose and throat examination, electrocardiograms, and bone marrow studies were normal. Bronchoscopy (performed before therapy was started) revealed an inflamed left bronchial tree. Blood and urine studies, agglutination tests and examination for acid-fast bacilli were negative. PPD number 1 and histoplasmin number 2 skin tests were positive. Sputum cultures revealed *N. pharyngis*, non-hemolytic *Staphylococcus albus*, and gamma streptococci. Gastrointestinal and sinus roentgen studies were negative. Chest films revealed increased markings in the area of the lingula, with retraction of the greater fissure and adjacent thickened pleura anteriorly on the left. On Jan. 7, 1957, a 3-cm. consolidation appeared in the right middle lobe, clearing by Jan. 14. The bronchogram is in Figure 2. The patient continues symptomatic at the present time.

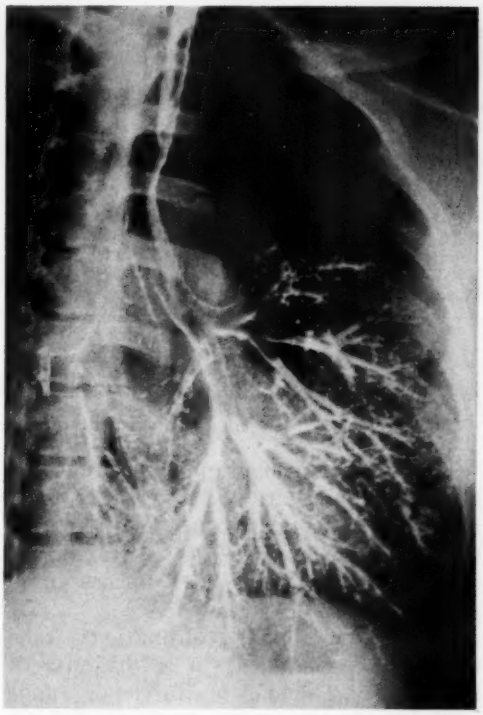

Fig. 2. Case II. Bronchogram demonstrating early involvement of the bronchial glands in the left upper lobe bronchus. The otherwise normal bronchial tree is noteworthy.

SUMMARY

A bronchographic sign of chronic bronchitis—glandular involvement of the bronchial mucosa—with 2 illustrative cases is presented. To our knowledge this has not been previously described in the American radiological literature; therefore, a brief review of the pertinent European literature is added.

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REFERENCES

1. ELWI, A. M., AND EL-WARRAKI, S.: A Pathological Study of Bronchial Inflammation. J. Egyptian M. A. **36**: 49–58, 1953.

2. FISCHER, F. K.: Beitrag zur Kenntnis der Veränderungen im Bronchogramm bei chronischer Bronchitis. Fortschr. a. d. Geb. d Röntgenstrahlen **72**: 653–659, April 1950.

3. GUDBJERG, C. E., AND THOMSEN, G.: Inflammatory Changes in the Bronchial Glands in Chronic Bronchitis, Demonstrated Bronchographically. Acta radiol. **42**: 269–275, October 1954.

4. KNOTT, J. M. S., AND CHRISTIE, R. V.: Radiological Diagnosis of Emphysema. Lancet **1**: 881–883, April 21, 1951.

5. LISTER, W. A.: Chronic Bronchitis: Never a Complete Diagnosis. Lancet **1**: 719–721, April 30, 1949.

6. MORLOCK, H. V., AND PINCHIN, A. J. S.: Bronchial Diverticulosis. Lancet **2**: 236–237, July 29, 1933.

7. OSWALD, N. C., HAROLD, J. T., AND MARTIN, W. J.: Clinical Pattern of Chronic Bronchitis. Lancet **2**: 639–643, Sept. 26, 1953.

8. REID, L. M.: Demonstration at 46th Annual General Meeting of the Association of Physicians of Great Britain and Ireland, 1952.

9. REID, L. M.: Pathology of Chronic Bronchitis. Lancet **1**: 275–278, Feb. 6, 1954.

10. SICARD, J. A., AND FORESTIER, J.: Méthode générale d'exploration radiologique par l'huile iodée. Bull. et mém. Soc. méd. d. hôp. de Paris **46**: 463–469, March 17, 1922.

11. SIMON, G., AND GALBRAITH, H. J. B.: Radiology of Chronic Bronchitis. Lancet **2**: 850–852, Oct. 24, 1953.

12. STILLER, H.: Die Bedeutung der Bronchographie für die Chirurgie. Arch. f. klin. Chir. **262**: 546, 1949.

13. STUTZ, E.: Bronchographische Beobachtungen beim Husten. Klin. Wchnschr. **26**: 536–540, Sept. 1, 1948.

SUMMARIO IN INTERLINGUA

Un Signo Bronchographic de Bronchitis Chronic

Un signo bronchographic de bronchitis chronic es describite que pare haber essite reportate previemente in le litteratura europee solmente. Illo consiste in un affection del glandulas del mucosa bronchial.

Roentgenogrammas routinari es relativemente pauco utile in le diagnose de bronchitis. Tamen, le bronchogramma non solmente exclude altere conditiones sed es etiam capace in un alte procentage del casos a revelar le effectos del processo irritative per replenar le ductos dilatate del glandulas mucose. Istos age como un specie de latrina pro le stagnante secretiones e permitte a infectiones secundari penetrar plus profundemente in le parietes bronchial e destruer histos in semper plus grande quantitates.

Es reportate duo casos illustrative.

The Angled Postero-anterior Projection of the Stomach[1]

An Attempt at Better Visualization of the High Transverse Stomach

SEWELL S. GORDON, M.D.

MOST RADIOLOGISTS would agree that the high transverse stomach is the type most difficult to examine. In the first place, this situation is most frequently encountered in the very obese patient, in whom fluoroscopic visualization is difficult on the basis of body thickness alone. In the second place, this type of stomach lies under the costal margin and is therefore inaccessible to palpation. Even more significant is the fact that there is considerable overlapping of the various portions of the stomach thus situated, so that fairly large segments may be completely obscured from clear observation. Occasionally, despite the use of multiple projections, parts of the contour of the stomach, particularly in the region of the upper corpus, elude full visualization. All of these considerations limit diagnostic accuracy.

With this problem in mind, the author has utilized a new projection to minimize the amount of overlapping of the various portions of the stomach. This projection has the virture of "opening up" the stomach, so to speak, by projecting the fundus and upper portion of the body (proximal segment) upward and the antrum and lower portion of the body (distal segment) downward, relatively, so that the appearance is much the same as in the ordinary sthenic individual. On review of the literature, no reference to the use of such a projection could be found.

The present report is offered as a preliminary evaluation of the technic. It has been employed in an occasional case for about three years, and recently has been made a routine in all patients with a high transverse stomach. It is hoped that, with more general utilization, a more complete evaluation may be made. Up to the present time there have been only isolated instances in which the projection made possible a diagnosis which was not otherwise apparent either at fluoroscopy or on routine roentgenographic study. There have been cases, however, in which it gave considerable anatomical detail concerning the extent of a carcinoma or the localization of a benign gastric ulcer. On a few occasions it was useful in confirming an otherwise equivocal diagnosis.

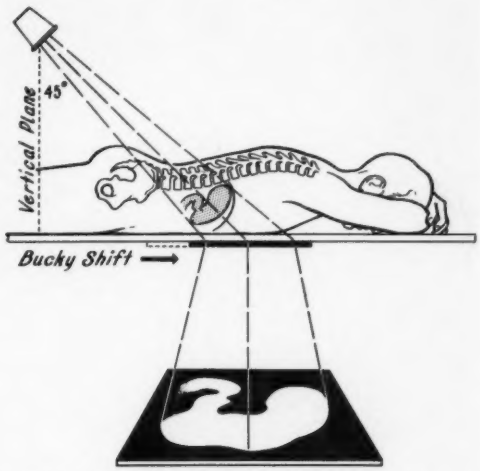

Fig. 1. Diagram of technic. For purposes of illustration a particularly high transverse stomach was not used. Note that the 45° angle beam approaches the perpendicular in relation to the "proximal" stomach used in this illustration. Note also the greater relative distortion of the more posteriorly located portions of the stomach.

TECHNICAL ANALYSIS

The problem is that of visualizing a stomach which lies in the plane of the x-ray beam rather than at right angles to it. In this situation demonstration of the margins of the stomach is not simple. The anterior and posterior walls may be seen in the true lateral or oblique projections as the upper and lower margins. The lesser and greater curvatures, however, may be observed tangentially only by a beam which parallels

[1] From the Veterans Administration Hospital, Minneapolis, Minn. Accepted for publication in March 1957.

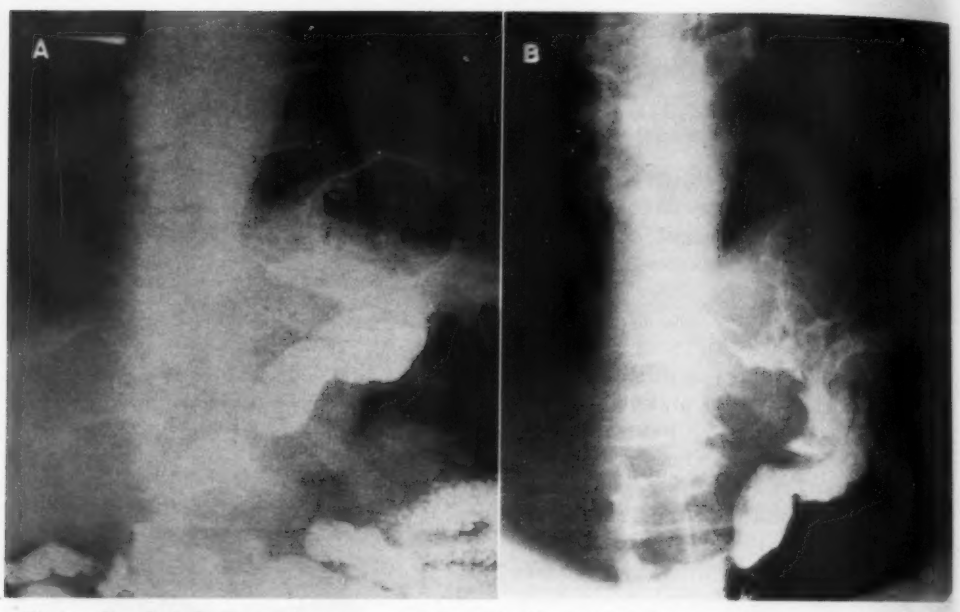

Fig. 2. Case I. A. In the routine postero-anterior projection, the stomach can be recognized as abnormal, but is otherwise hard to evaluate.
B. The angled projection shows the extent of involvement of the stomach and esophagus by carcinoma.

the longitudinal axis of the body. Since, for obvious reasons, this cannot be attained, it seemed advisable to approach the right angle as nearly as possible. For practical purposes, an angle of 45° is about the maximum for conventional equipment. In the obese patient even this angle has been sufficiently discouraging to the technicians to prompt them to adopt a 35° angle more or less on their own.

In a subject of average proportions with a high transverse stomach, the 45° angle does not offer much difficulty, but in the heavy-set patient the problem of getting a clear roentgenogram is considerably greater. There is no doubt, however, that with high kilovoltage and improved Bucky technic, greater angles, perhaps even up to 55°, would not pose too great a problem. It may be mentioned, in this connection, that the routine right anterior oblique projection could be improved diagnostically by using angulation of the tube in the same way.

In actual practice the patient is positioned in precisely the same manner as for the routine postero-anterior projection of the stomach. A 14 × 17-inch cassette in the Bucky tray is pushed upward so that its upper end is at the level of the chin. The tube is tilted 45° toward the head and centered to the middle of the cassette. The target-film distance is 36 inches. Average technical factors are 100 kv, 200 ma, 0.6 second.

CASE PRESENTATIONS

A few cases have been selected to demonstrate the usefulness of the angled projection.

CASE I (Fig. 2): J. J. T., a 71-year-old white male, was seen with dysphagia and weight loss of three months duration. He had been given five transfusions for anemia before admission. Except for pallor and evidence of weight loss, physical examination was negative.

Laboratory data: Hemoglobin 16 gm.; no free acid on gastric analysis; stools 4+ for occult blood.

An *upper gastrointestinal study* Feb. 10, 1956, revealed a massive carcinoma of the stomach involving the fundus and upper half of the body, with evidence of involvement of the terminal 2 cm. of the esophagus. The extent of the lesion was best demonstrated on the angled projection.

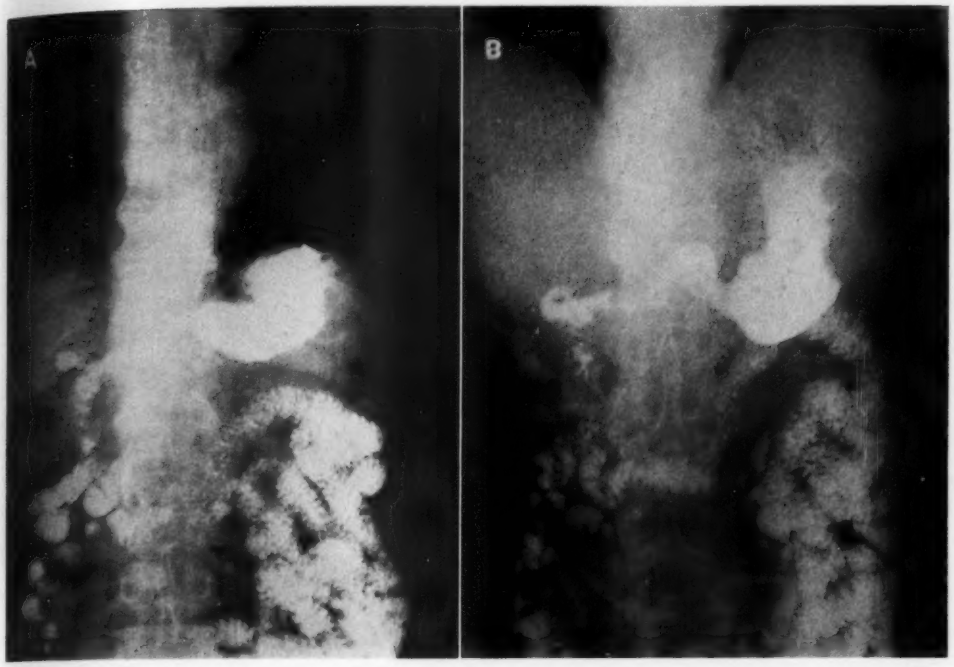

Fig. 3. Case II. A. A routine postero-anterior projection shows irregularity of the greater curvature of the stomach which could be dismissed as due to enlarged folds.
B. The angled projection demonstrates carcinoma involving both curvatures.

At *surgery* a carcinoma of the proximal half of the stomach was found, with lymphadenopathy along the entire lesser curvature but no evidence of distant or hepatic metastasis. A total radical gastrectomy, including the terminal esophagus, was performed. Microscopically, several lymph nodes along both the lesser and greater curvatures were involved by tumor. The patient did well postoperatively.

Comment: On the routine postero-anterior projection, the gross distortion of the stomach was recognized, but analysis was made difficult by marked shortening and retraction. On the angled projection, involvement of the esophagus as well as the extent of the lesion in the stomach was clearly demonstrated.

CASE II (Fig. 3): J. B., a 66-year-old white male, complained of increasing weakness and inability to walk for three weeks prior to admission. There was a history of a previous cerebrovascular accident with residual paretic symptoms in the right leg. The patient had lost 25 pounds recently, despite a good appetite. He had received blood transfusions and multiple vitamins for anemia. He appeared older than his stated age and there were neurological changes consistent with cerebrovascular accident.

Laboratory studies: Hemoglobin 13.5 gm., sedimentation rate 53 mm. in one hour, stools negative for occult blood. Gastric analysis showed no free acid, and the Schilling test suggested a diagnosis of pernicious anemia.

An *upper gastrointestinal study* showed a large carcinoma of the stomach involving the greater and lesser curvatures. The extent of the lesion was best appreciated on the angled projection.

At *surgery* the carcinoma was found to involve a large portion of the posterior wall and to extend to both curvatures, more so to the greater. Widespread metastases were present in the abdomen. A radical resection was not done.

Comment: The greater curvature involvement was suspected on the routine postero-anterior projection, but no definite diagnosis could be made. On the angled projection the diagnosis was simplified and the extent of the lesion along both curvatures was well defined.

CASE III (Fig. 4): E. L., a 75-year-old white female, had a one-year history of post-prandial upper abdominal distress, consisting of heartburn, bloating, and limited stomach capacity. She had lost 25 pounds in the last four months. On examination she

Fig. 4. Case III. A. A postero-anterior projection reveals no evidence of a lesion.
B. The angled projection shows a benign gastric ulcer at the incisura. This had been missed three times at fluoroscopy and was recognized on the third study only in this projection.

appeared slightly pale. One examiner described a probable epigastric mass.

Laboratory studies: Hemoglobin 14 gm.; 75 degrees of free acid on gastric analysis.

Two *upper gastrointestinal studies* done in July 1956 at another hospital were reviewed. Some questionable stiffness and ulceration in the pylorus were mentioned in the report. On re-examination at this hospital on Aug. 1, 1956, the fluoroscopist noted only pyloric deformity. The ulcer along the lesser curvature of the stomach at the incisura could be seen only on the roentgenogram made with the angled projection.

The patient did well on ulcer management and when last heard from had no complaints relative to the stomach.

Comment: In this case two previous x-ray studies of the stomach had failed to reveal the ulcer. Even on the third examination, it was not seen fluoroscopically or on routine films. Only on the angled projection was it demonstrable. Not only was this view of value in establishing the diagnosis, but it also showed the antral deformity to be due to spasm secondary to the ulcer at the incisura.

SUMMARY

A new projection has been used for better demonstration of the high transverse stomach. Technical considerations have been discussed. Several cases have been presented briefly to illustrate its field of usefulness. It is hoped that with more general utilization its value will be established.

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SUMMARIO IN INTERLINGUA

Le Angulate Projection Postero-Anterior del Stomacho

Es describite un nove projection angulate que meliora le demonstration del stomacho supero-transverse. Le uso del methodo es illustrate per tres casos.

Pro iste projection le patiente es positionate como in routinari examines postero-anterior del stomacho. Un cassetta de 14 per 17 pollices in le quadro de Bucky es pulsate in alto de maniera que su margine superior es al nivello del mento. Le tubo es basculate a 45° verso le capite e centrate super le centro del cassetta. Le distantia inter pecia de concentration e pellicula es 36 pollices. Iste projection ha le effecto de "aperir" le stomacho—a si dicer—per projicer le fundo e le portion superior del corpore (le segmento proximal) in alto e le antro e le portion inferior del corpore (le segmento distal) in basso.

Le extension de massive carcinoma gastric esseva ben demonstrate per le nove projection in 2 casos. In un tertie caso le methodo revelava un ulcere al longo del curvatura del stomacho, precisemente al incisura, ubi illo non haberea essite demonstrabile per altere medios.

Renografin as a New Contrast Medium for Cerebral Angiography

Report of Animal Experiments[1]

DAVID J. LaFIA, M.D., and RUDOLPH JAEGER, M.D.

RENOGRAFIN is a new contrast agent for cerebral angiography originating in Germany, where it is known as Urografin. A study of this new medium has been made on dogs.

Fig. 1. Angiogram obtained with Renografin 60 per cent

MATERIALS AND METHODS

Renografin (2) is an organic iodide with three atoms of iodine in each molecule. Its aqueous solution is a mixture of sodium and methylglucamine salts of 3,5-diacetylamino-2,4,6-tri-iodobenzoic acid. It has a molecular weight of 613.8; 62.1 per cent iodine content; *p*H 7.2 to 7.6; specific gravity 1.422.

Twelve experiments were done on 12 mongrel dogs weighing 7 to 10 kg. Under intraperitoneal pentobarbital anesthesia (35 mg. per kg.), either common carotid artery was cannulated with polyethylene tubing and ligated proximally. This was considered safe, since the vertebral artery and opposite carotid artery provide adequate blood supply. Renografin, 60 per cent, was injected in 5 c.c. amounts for various totals, as shown in Table I. To determine changes in the blood-brain barrier, Broman's (3) dye-indicator method with trypan blue was used, a total of 100 c.c. of the dye being given intravenously before, during, and after intracarotid injection of the contrast agent.

In one group of experiments the cerebral cortex was exposed for observation of *in vivo* changes in the blood-brain barrier, as well as effects on the pial vessels, following direct application of the contrast material to the cortex. In all experiments the brains were fixed by intracarotid inject of formalin. For study of the irritative effects on soft tissue, Renografin was injected around the carotid sheath, and one week later the area was inspected.

[1] From the Laboratory of Neurosurgical Research, Jefferson Medical College of Philadelphia, Philadelphia 7, Penna. Accepted for publication in April 1957.

This work was aided by a grant from the Squibb Institute for Medical Research. Renografin was supplied by Squibb & Co.; Hypaque and Diodrast by Winthrop Laboratories.

Figs. 2–4. Angiograms obtained with Thorotrast (Fig. 2), Hypaque 50 per cent (Fig. 3), and Diodrast 35 per cent (Fig. 4) in similar amounts.

TABLE I: TOXICITY OF RENOGRAFIN (60 PER CENT)

Exp.	Total Amount (c.c.)	Fits	Death	Breakdown of Blood-Brain Barrier (staining)
1	25	None	No	No
2	50	None	No	No
3	15	None	No	No
4	20	None	No	No
5	75	None	No	No
6	50	Generalized	Yes	Diffuse
7	65	None	No	No
8	70	None	No	No
9	100	None	No	No
10	120	None	Yes	Diffuse
11	140	None	Yes	No
12	160	None	Yes	Diffuse

RESULTS AND COMMENTS

The experimental results are summarized in Table I. Toxicity was appraised on the basis of (*a*) death of the animal, (*b*) fits, (*c*) break-down of blood-brain barrier and (*d*) irritation of cortex and soft tissues.

Three dogs were allowed to live for one week after intracarotid injection of Renografin: 1 of these received 25 c.c., another 50 c.c., and the third 75 c.c. In none were there apparent ill effects. In acute experiments with 9 dogs, amounts up to 100 c.c. were tolerated except in Experiment 6, when death followed the use of 50 c.c. In this instance the brain was severely swollen. Effects on the blood-brain barrier were not consistent. Staining indicative of break-down of the barrier occurred after 120 c.c. and 160 c.c., but not after 140 c.c. There was no apparent correlation between break-down of the barrier and fits, except in Experiment 6, in which death occurred. *Irritation* was minimal. When the medium was injected into the soft tissues of the neck, scar formation was mild. Applied directly to the cerebral cortex, it caused neither fits nor changes in the caliber of pial vessels.

Comparative radioopacity was evaluated by obtaining carotid arteriograms with Renografin, Thorotrast, Hypaque 50 per cent, and Diodrast 35 per cent (Figs. 1–4). The same dog was used for each arteriogram and care was taken to observe identical technic for each agent. Ten minutes were allowed between injections to eliminate possible vasospasm.

CONCLUSIONS

The following statements are valid for dogs, but not for man.

1. Except for its safety in large amounts (average of 8 c.c. per kilogram of body weight), Renografin adds little new to the field of contrast media for cerebral angiography. As an organic iodide, it still carries the threat of anaphylactoid reaction, as is suggested by Experiment 6, in which 50 c.c. caused severe edema, fits, and death of the dog.

2. Renografin produced no demonstrable irritation of the cerebral cortex or soft tissues.

3. Renografin (60 per cent) affords as good a contrast as Thorotrast and Hypaque, and better contrast than Diodrast 35 per cent.

SUMMARY

Renografin is a new tri-iodinated compound for cerebral angiography. It was tested in experiments on 12 dogs to find out whether it would (*a*) kill the animal, (*b*) cause fits, (*c*) alter the blood-brain barrier, (*d*) produce a good arteriogram. The compound was injected into the carotid artery, effects on the brain cortex were directly observed, and changes in the blood-brain barrier were recorded by the trypan blue indicator method. In 11 of 12 dogs the medium proved to be safe in amounts up to 100 c.c.; 1 dog died after injection of 50 c.c. Arteriograms in dogs made with Renografin were as good as those obtained with Thorotrast and Hypaque, and better than those with Diodrast 35 per cent.

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REFERENCES

1. GROTE, W., AND BETTAG, W.: Beitrag zur Anwendung des Urografins bei der zerebralen Angiographie. Fortschr. a. d. Geb. d. Röntgenstrahlen **83**: 579–583, October 1955.

2. Contrast Medium for Angiography. Squibb Institute for Medical Research. Unpublished.

3. BROMAN, T.: The Permeability of the Cerebrovascular Vessels in Normal and Pathological Conditions. Copenhagen, E. Munksgaard, 1949.

SUMMARIO IN INTERLINGUA

Renografin, un Nove Medio de Contrasto pro Angiographia Cerebral
Reporto de Experimentos Animal

Renografin es un nove composito triiodate pro angiographia cerebral. Illo esseva probate in 12 experimentos con 12 canes pro determinar si illo (1) occideva le animal, (2) causava convulsiones, (3) alterava le barriera sanguino-cerebral, e (4) produceva un bon arteriogramma. Le composito esseva injicite in le arteria carotic. Effectos in le cortice cerebral esseva observate directemente. Alterationes in le barriera sanguino-cerebral esseva registrate per medio del methodo a blau trypan como indicator. In 11 ex 12 canes, le composito se monstrava salve in quantitates usque a 100 cm^3; 1 can moriva post 50 cm^3. Arteriogrammas ab canes facite con Renografin esseva tanto bon como le arteriogrammas obtenite con Thorotrast e Hypaque e melior que illos obtenite con 35 pro cento de Diodrast.

Flow Rates of Contrast Substances Obtainable at Conventional Angiocardiography[1]

ROBERT N. COOLEY, M.D.

CONVENTIONAL angiocardiography for visualization of the thoracic aorta has been abandoned in favor of aortography by some workers (4–7) because of their inability to obtain, consistently, angiocardiograms which adequately delineate abnormalities in this area. The quality of the angiocardiographic image is affected by many factors, such as the heart size, the amount of residual blood within the heart, the site of injection of the contrast substance, the size of the thorax, radiographic exposure factors, and, of considerable importance, the flow rate or speed with which the contrast substance is introduced into the venous side of the circulation. The purpose of this paper is to consider some of the factors which affect the speed of injection of contrast substances for conventional angiocardiography in adults.

Dotter and Steinberg (1) state that an injection time for contrast substance greater than one and one-half seconds may lead to a technically unsatisfactory angiocardiogram. Robb and Steinberg (6) indicate that the upper permissible limit is two seconds. If 40 to 50 c.c. of Diodrast be accepted as a proper dose for adults, it can be calculated that a flow rate of approximately 9 to 12 gm. of iodine per second and a total of 14 to 17 gm. per injection are the minimum basic requirements for satisfactory results. The use of 70 per cent Urokon, with its increased iodine content, facilitates attainment of these basic dose levels and flow rates.

The importance of proper injection technics, with the Robb syringe and cannulas, has been re-emphasized by Steinberg and Finby (8) and must be stressed. Improper holding and/or positioning of the syringe and cannula in relation to the vein may produce kinking or angulation and thus obstruct the inflow of contrast substance; incorrect alignment may prevent maximum force from being applied, or the force may be poorly directed so that the plunger tends to bind during the latter part of its course of travel.

Dotter and Steinberg (1) have a picture of the proper position of the syringe and cannula in their book on angiocardiography (page 13). The left hand grips the syringe near the hub and also includes the proximal end of the cannula so as to maintain rigidity and correct alignment in relation to the vein under the stress of the injection. The force applied to the plunger is delivered through the thumb of the right hand, the middle and index fingers being used as an anchor. Toward the end of the injection it is necessary to bring the forearm into play to reinforce the thumb. Some operators apply force to the plunger with both thumbs. Obviously more force can be applied in this manner, but whether the flow rate is significantly increased has not been determined. A "two-thumb" injection can be quite successful, but the risk of disturbing the alignment of the cannula with the vein, thus producing an obstruction, is so great that this technic is generally inadvisable.

Another technical error may consist in failure to have the syringe barrel and plunger scrupulously clean. The plunger should be cleansed with sterile gauze, and the syringe tested for smoothness of operation prior to the actual injection. Any crystalline residuum from previous injections must be carefully washed away by rinsing with sterile saline. Proper heating of the contrast substance not only reduces precipitation of crystalline material within the syringe, but also lessens viscosity and thus increases injection speed. The injection should be given during slow inspiration. Also, the patient must be

[1] From the University of Texas, Medical Branch, Galveston, Texas. Accepted for publication in March 1957.

cautioned against straining or producing a Valsalva effect, particularly before all of the contrast substance has been introduced, as this tends to prevent its entering the thorax. Finally, there is no substitute for experience and familiarity with proper positioning, elevation of the arm, and timing of the injection.

Ninety per cent Miokon and 90 per cent Hypaque (3) are now under investigation as to their suitability for angiocardiography. These high concentrations were developed with the object of delivering an increased amount of iodine per second into the blood stream while taking advantage of the supposedly innocuous side effects of these media. The iodine content of Miokon 90 per cent,[2] is approximately 0.45 gm. per cubic centimeter; of Hypaque 90 per cent, approximately 0.46 gm. per cubic centimeter;[3] and of Urokon 70 per cent, approximately 0.46 gm. per cubic centimeter.[4] The 90 per cent solutions, both Miokon and Hypaque, were found on inspection to be much more viscous at room temperatures than Urokon 70 per cent. This increased viscosity materially affects the flow rates obtainable at angiocardiography. To determine the effect of heat on the viscosity and flow rate of one of these more concentrated solutions, namely Miokon 90 per cent, is one of the objects of the present study.

Flow rates for Urokon 70 per cent through Cournand and Lehman catheters, with the Gidlund pump, have been published by Kjellberg *et al.* (5). v. Euler (2) has presented the variations, at different temperatures, in the flow rate of Perabrodil, 35 and 50 per cent, Thorotrast, and Uroselectan B. No data, however, could be found concerning the flow rates of any of the commonly used contrast substances introduced by the conventional Robb syringe and cannulas of various sizes, and at injection pressures that might be expected to prevail during hand-powered angiocardiography.

[2] Miokon was supplied by the Mallinckrodt Chemical Works, St. Louis, Mo.

[3] Information obtained from folders supplied by Winthrop Laboratories.

[4] Information obtained from folders supplied by the Mallinckrodt Chemical Works, St. Louis, Mo.

PROCEDURES AND MATERIALS

The following materials were employed:

1. Robb 50 c.c. (B-D) syringe with a plunger 26 mm. in diameter.
2. Four Robb cannulas, 15 gauge (0.045 in.), 13 gauge (0.074 in.) 12 gauge (0.085 in.), and 10 gauge (0.105 in.)
3. Mercury Manometer with attached tubing, and adapters.
4. Stop watch.
5. 90 per cent Miokon.
6. 70 per cent Urokon (Stock solution).
7. Tap water.
8. Water bath.
9. Darkroom thermometer.

Maximum possible injection pressures, determined with the use of a closed air system and a mercury manometer, were equivalent to about 13 pounds per square inch when both thumbs were employed and about 10 pounds per square inch with one thumb. However, no system that measures pressures during actual injection without decreasing the injection speed, has yet been devised, although such pressures are probably 8 to 10 pounds per square inch. The important consideration is that the injection pressures are those that would be used under the actual circumstances surrounding angiocardiography. All injections, performed by the author, who is a person of moderate strength, were done with the maximum force that he was capable of applying, and it is believed that the force in all instances was comparable. For determination of discharge times a stop watch graduated in one-tenth seconds was used, the time-keeper having been trained with numerous practice injections. Injection times thus determined are thought to be accurate to a tenth of a second. In obtaining discharge times for this report the mean of ten discharges, calculated to the nearest tenth of a second, has been used.

Discharges were made into free air, but the contrast fluid was collected in a large pan kept at the required temperature by a water bath. Customarily, two injections were made, with solutions freshly aspirated

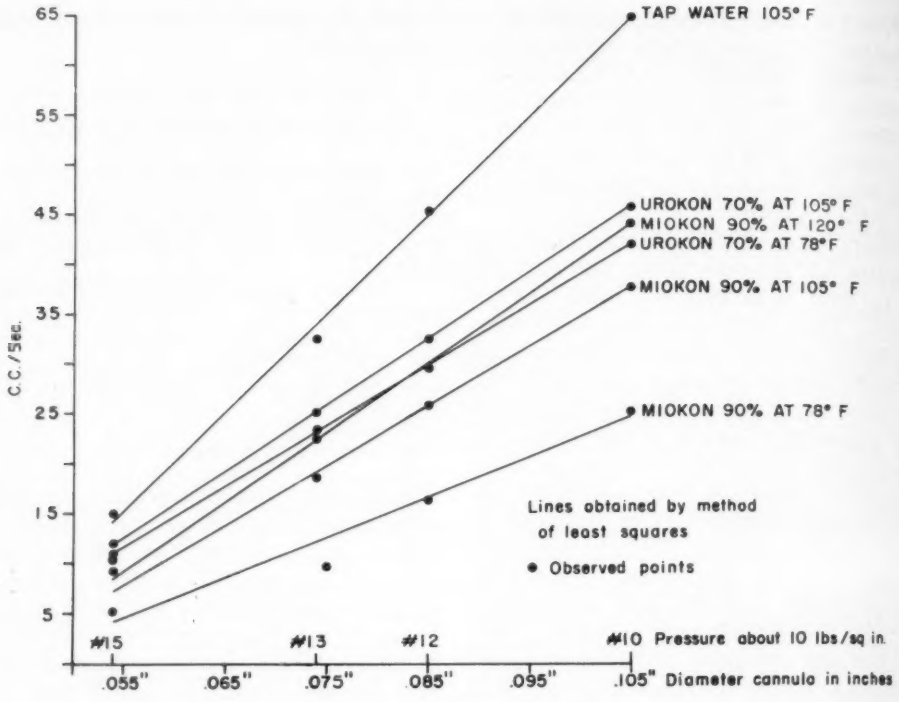

Fig. 1. Flow rates for tap water, Urokon 70 per cent and Miokon 90 per cent at the indicated temperatures, using a standard Robb syringe and cannulas of indicated size.

from the original container. The remaining eight injections in each case were made with solution caught in a large pan and kept at the designated temperature. Temperatures given are those of the water bath in which the contrast substance was submerged for a period of at least ten minutes. The air temperature of the room in which the contrast substance was stored was 78°. While it is true that flow rates obtained with a free, unattached syringe and cannula may not be entirely valid for angiography as it is usually performed, it is the author's experience that the two procedures are closely comparable if in actual practice the proper injection technic is used, the venous pressure is in the normal range, and the patient is co-operative. Certainly, the flow rates obtained with the free unattached syringe and cannula are maximum and could not be exceeded under any conditions associated with the actual procedure.

Initially, 30 discharges were made with a one-thumb technic, and an additional 30 with a two-thumb technic. Cannulas of various sizes were used. The difference in injection time was of the order of one-tenth to two-tenths of a second in favor of the two-thumb technic where the total injection time was in excess of three seconds. Where the injection time was less than three seconds, no difference could be determined. Since a difference of one-tenth to two-tenths of a second in an overall injection time of two seconds is not of great significance, it was decided to carry out all of the remaining injections with the one-thumb technic.

RESULTS

As has been stated above, no significant difference in the injection time could be determined between a two-thumb and a one-thumb technic.

Figure 1 shows the flow rates with different size cannulas at varying tempera-

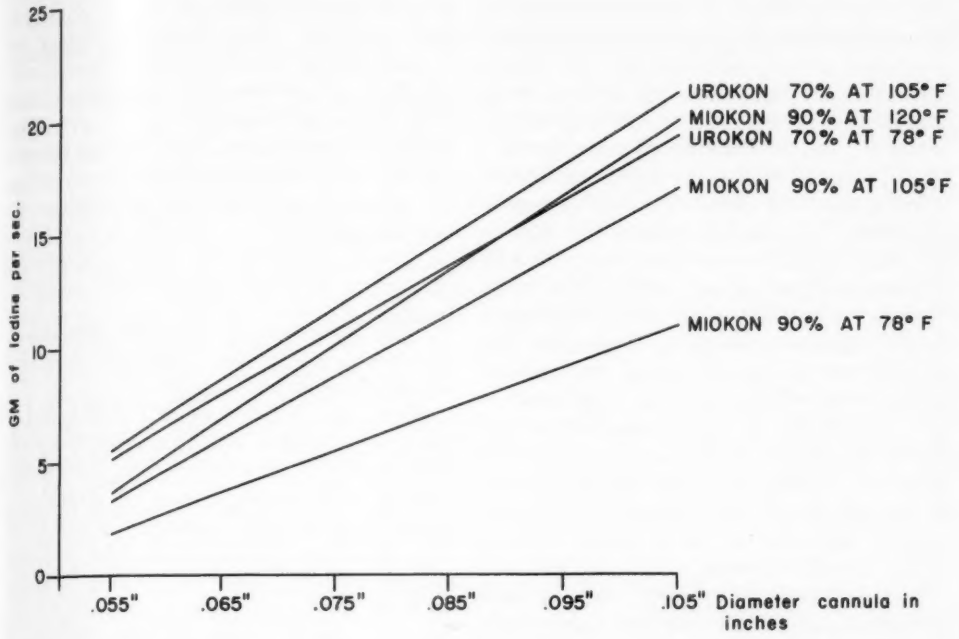

Fig. 2. Using the data from Fig. 1, grams of iodine injected per second for Miokon 90 per cent and Urokon 70 per cent have been calculated. Miokon 90 per cent contains approximately 0.45 gm./c.c. of iodine and Urokon approximately 0.46 gm./c.c.

tures for Miokon 90 per cent, Urokon 70 per cent, and tap water. The rate of flow is plotted against the diameter of the cannula. The solid dots represent observed flow rates; the lines joining them were obtained by the statistical method of least squares.[5] It is readily seen that both of the contrast substances are more viscous than water and that Urokon 70 per cent is less viscous than Miokon 90 per cent. The maximal injection speed that can be obtained with Urokon 70 per cent at a temperature of 105° and a No. 12 cannula is about 33.5 c.c. per second (15.4 gm.I/sec.), which would give an injection time of one and a half seconds for 55 c.c. of contrast substance. Also, 15.4 gm. I/sec. is considerably greater than the 11.7 gm. I/sec. accepted as the minimum permissible flow. Thus, the period that is usually accepted as the maximum allowable injection time is easily attained using Urokon 70 per cent.

[5] The graphs are actually curves that approximate straight lines in the segments under consideration.

By heating Urokon 70 per cent from 78° (room temperature) to 105°, the flow is increased by about 2.5 c.c. per second. This improvement in injection speed is not as significant as that found with Miokon 90 per cent but is still sufficient to make the routine heating of Urokon 70 per cent for injection desirable. The heating, of course, prevents the precipitations of crystalline contrast substance.

The change in the viscosity of Miokon upon heating is more striking. At room temperature, with a No. 12 cannula, the flow rate of only about 11.5 c.c. per second (5.2 gm. I/sec.) could be expected; this would give an injection time for 50 c.c. of about four and a half seconds. This unquestionably would lead to an unsatisfactory angiocardiogram. By heating the Miokon to 105°, the injection time could be reduced to about two seconds, which would probably provide a satisfactory result. If, however, the Miokon is heated to 120° a flow rate of about 30 c.c. per second (13.5

gm. I/sec.) is obtained, which should provide a satisfactory concentration of contrast substance in the left side of the heart. Since the effects of heating become more pronounced as the size of the cannula is increased, the desirability of using even a No. 10 cannula where possible is indicated.

In Figure 2 the grams of iodine per cubic centimeter are plotted against the size of the cannula. Here it is seen that Miokon 90 per cent, even at temperatures of 120°, will deliver less iodine per cubic centimeter than Urokon 70 per cent. However, the increase in grams of iodine per second achieved by heating Miokon 90 per cent is such that densities approaching those obtained with Urokon 70 per cent should be obtained. While we have not as yet injected Miokon at 120° temperature into a patient, we have reason to believe that it would be well tolerated.

Contrast substance at 120° can be successfully handled and tolerated by the bare hand.

DISCUSSION

It is apparent that the maximum injection time mentioned by Dotter and Steinberg (1) for contrast substance in angiocardiography is approximately the shortest time possible where 50 c.c. of contrast substance are used with a No. 12 cannula. In other words, a period of one and a quarter to one and a half seconds is the best that can be hoped for. Experience has shown that in a majority of adult patients this injection time will be adequate, although the factors of heart size and residual blood in the heart will still be important. Heating of all of the contrast substances is necessary, but the effect of heating is much greater with a more concentrated substance, such as Miokon 90 per cent. It is probable that heating to a temperature of 120° F. is desirable for Miokon 90 per cent although as yet this temperature has not been used in practice. This should be investigated further. It can be seen, however, that Miokon at 120° F. will not deliver quite the number of grams of iodine per second that can be obtained with Urokon 70 per cent and therefore cannot be expected to give a better contrast or denser angiographic shadow. The main advantage of Miokon 90 per cent is, of course, that its side effects are considerably less pronounced than those of Urokon 70 per cent. This particular possibility is now under investigation. The importance of strict adherence to proper injection technic cannot be overemphasized.

SUMMARY

The flow rates of contrast substances necessary to produce satisfactory angiocardiograms are reviewed.

Flow rates for tap water, Urokon 70 per cent, and Miokon 90 per cent at temperatures from 78° to 120° F. have been determined, with varying sizes of Robb cannulas and a Robb syringe. From these data, the number of grams of iodine per second that it is possible to deliver under each set of circumstances has been plotted. Various factors concerning the technics of injections in angiocardiography have been discussed.

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REFERENCES

1. DOTTER, C. T., AND STEINBERG, I.: Angiocardiography. Annals of Roentgenology, Vol. XX. New York, Paul B. Hoeber, Inc., 1951.
2. v. EULER, H. E.: Die peroesophageale Aortenpunktion, ihre diagnostischen und therapeutischen Möglichkeiten. Arch. Ohren- Nasen- u. Kehlkopfh. **155**: 536–567, 1949.
3. FINBY, N., POKER, N., AND EVANS, J. A.: Ninety Per Cent Hypaque for Rapid Intravenous Roentgenography. Preliminary Report. Radiology **67**: 244–245, August 1956.
4. JÖNSSON, G., BRODÉN, B., AND KARNELL, J.: Thoracic Aortography with Special Reference to its Value in Patent Ductus Arteriosus and Coarctation of the Aorta. Acta radiol. suppl. 89, 1951.
5. KJELLBERG, S. R., MANNHEIMER, E., RUDHE, U., AND JÖNSSON, B.: Diagnosis of Congenital Heart Disease. A Clinical and Technical Study by the Cardiologic Team of the Pediatric Clinic of Karolinska Sjukhuset, Stockholm. Chicago, Year Book Publishers, Inc., 1955.
6. ROBB, G. P., AND STEINBERG, I.: Visualization of the Chambers of the Heart, the Pulmonary Circulation and the Great Blood Vessels in Man; A Practical Method. Am. J. Roentgenol. **41**: 1–17, January 1939.
7. SLOAN, R. D., AND COOLEY, R. N.: Coarctation of the Aorta. The Roentgenologic Aspects of One Hundred and Twenty-Five Surgically Confirmed Cases. Radiology **61**: 701–721, November 1953.
8. STEINBERG, I., AND FINBY, N.: The Importance of Angiocardiography for Visualizing the Thoracic Aorta. Arch. Surg. **74**: 29–38, January 1957.

SUMMARIO IN INTERLINGUA

Velocitate Injectori de Substantias de Contrasto Effectuabile in Angiographia Conventional

Le autores studiava certes del factores que affice le velocitate injectori de substantias de contrasto usate in angiocardiographia con subjectos adulte. Le medios usate esseva 90 pro cento de Miokon e 70 pro cento de Urokon. Le temperaturas variava inter 78 F del ambiente e 120 F.

Esseva constatate que 70 pro cento de Urokon es minus viscose que 90 pro cento de Miokon. Ambes esseva plus viscose que aqua ordinari. Le velocitate maximal effectuabile in le caso de 70 pro cento de Urokon, a un temperatura de 105 F e con un cannula No. 12, esseva circa 33,5 cm^3 per secunda (i.e. 15,4 g de iodo per secunda) o 55 cm^3 in un secunda e medie. Le calefaction a 105 F accelerava le fluxo de 70 pro cento de Urokon per circa 2,5 per secunda in comparation con le fluxo al temperatura normal del ambiente.

In usar un cannula No. 12 sub le conditiones del temperatura del ambiente, un fluxo de Miokon de circa 11,5 cm^3 per secunda poteva esser expectate. Isto resultarea in un tempore injectori de circa quatro secundas e medie pro 50 cm^3. Per calefacer Miokon a 105 F, il esseva possibile reducer le tempore injectori a circa duo secundas. Isto resultarea probabilemente in un angiocardiogramma satisfactori. Sed quando Miokon esseva calefacite a 120 F, le fluxo esseva accelerate a circa 30 cm^3 per secunda (i.e. 13,5 g de iodo per secunda).

Miokon a iste temperatura non esseva usate in un patiente. On vide que Miokon a 120 F non livrarea integremente le mesme numero de grammas de iodo per secunda como es obtenibile in le caso de Urokon, e per consequente on non pote expectar que Miokon produce un contrasto melior o un plus dense umbra angiographic. Su principal avantage es que su effectos lateral es considerabilemente minus pronunciate que illos de Urokon.

Diffuse Thickening of the Calvarium in Osteogenesis Imperfecta

THEODORE E. KEATS, M.D.

RARELY, DIFFUSE thickening of the calvarium may be found in osteogenesis imperfecta, in contrast to the usual poor cranial development observed in that disease. In a case recently reported (1), of fragile bones and diffuse calvarial thickening in a child, the authors believed that the diagnosis of osteogenesis imperfecta could be excluded because of unusual widening of the medullary cavities of the unfractured bones, and because of the thickness of the calvarium. Though not entirely comparable, the following well documented case of osteogenesis imperfecta with a thickened calvarium would seem to offer a basis for a dissenting opinion and to emphasize the importance of recognizing that thickening of the skull may occur in osteogenesis imperfecta. This is believed to be the third such case to be reported.

CASE REPORT

M. K., a 28-year-old white married female, was admitted to the University of Missouri Medical Center on July 29, 1956, with fractures of the right femur and of the left tibia and fibula. The fractures were sustained following mild trauma eight days previously, when the patient's knee "gave way" and she fell to the floor. A history of repeated fractures was obtained: of the right elbow at a very early age; of the right arm, in two places, following a fall at the age of eight or nine years; of the left patella at the age of twenty-four.

The patient's father had blue sclerae, "soft bones," and a record of many fractures; her 33-year-old brother had not walked since the age of two because of "soft bones"; another brother, twenty-seven years old, had broken both patellae, both ankles, and one arm. Both of these brothers had blue sclerae. An eleven-year-old brother had never broken a bone and the sclerae were normal.

The patient had experienced difficulty in hearing since the age of thirteen. Her father and two oldest brothers also had hearing defects.

Physical examination on admission showed mild obesity, blue sclerae, deafness, a rather large head, and changes secondary to the fractures of the right femur and left leg. The menstrual history was normal.

The blood findings were as follows: hematocrit 32 per cent, white blood cells 11,750, platelets and erythrocytes normal, hemoglobin 11.0 gm., serum calcium 11.6 mg. per cent, serum inorganic phosphate 3.36 mg. per cent, albumin 3.0 gm. per cent, globulin 3.1 gm. per cent, plasma electrophoretic pattern normal, serologic test for syphilis negative, blood sugar 23.8 mg. per cent, non-protein nitrogen 23.8 mg. per cent. The specific gravity of the urine was 1.010. It was negative for albumin, sugar, and acetone. The Sulkowitch test on admission was 3+, probably due to the recent fractures and immobilization, with reversion to 2+ on re-examination two months later.

Roentgen examination on admission showed a comminuted fracture of the distal shaft of the right femur and fractures of the distal shafts of the left tibia and fibula. The femoral fracture was treated by intramedullary pinning, and the fractures of the left leg by closed reduction and application of a cast.

A roentgen skeletal survey showed a degree of generalized osteoporosis entirely out of keeping with the patient's age (Fig. 1). The cortices were not thinned and there were no residual deformities from earlier fractures. The skull was large and granular in appearance and showed marked uniform thickening of the frontal, parietal and occipital bones due to widening of the diploic space. There was some undulation of the inner table, but the outer plate was thin and well defined. The base of the skull and the facial bones were not remarkable. The frontal sinuses were large. The sella turcica was normal.

Sections of bone removed from the right femur at the time of insertion of the intramedullary pin were examined by Dr. Joseph E. Flynn, Professor of Pathology at the University of Missouri School of Medicine. His report is as follows:

"Sections of bone reveal a fatty marrow infiltrated by large mononuclears filled with phagocytized lipid. At first glance, they somewhat resemble Gaucher cells, but on closer examination the characteristic cytoplasmic wrinkling is absent. These cells are undoubtedly reactive elements, probably to trauma. Some of the bone contains bits of cortex. The spicules are narrow and widely separated. The entire cortex is markedly thinned. *Diagnosis:* Osteoporosis, compatible with osteogenesis imperfecta tarda."

From the Department of Radiology, The University of Missouri School of Medicine, Columbia, Mo. Accepted for publication in April 1957.

Fig. 1. Roentgenograms of the pelvis, forearm and hand, and thoracic cage, showing a degree of osteoporosis out of keeping with the age of the patient.

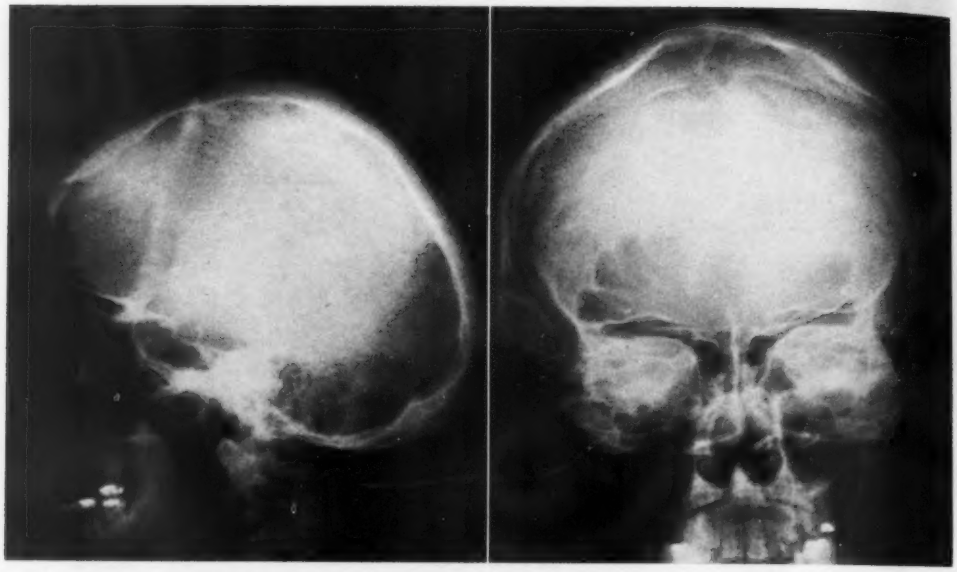

Fig. 2. Roentgenograms of the skull showing thickening of the calvarium and granular appearance of the bones.

DISCUSSION

The roentgen findings in classic osteogenesis imperfecta are well documented and need no amplification here. Caffey has pointed out that the different types of this disease, based on the age of onset and severity, are all variants and phases of the same basic condition (2).

Thickening of the calvarium is a rare manifestation. Fairbank, in his discussion of osteogenesis imperfecta, described a case with irregular hyperostoses of the frontal and parietal bones, affecting both inner and outer tables (3). This irregularity is in contrast to the diffuse widening of the diploic space in the patient reported by Bakwin and Eiger (1), and in our patient.

Bakwin and Eiger, as pointed out above, did not consider their case an example of osteogenesis imperfecta, because of the widened medullary cavities of the unfractured bones and the thickening of the calvarium. In Fairbank's case, however, the medullary cavities, including those of the hand, were widened. Our patient showed skull changes quite similar, though of less marked degree, to those described by Bakwin and Eiger. In view of these observations we believe that their case does not present any features which would prevent its inclusion in the group of osteogenesis imperfecta.

The case described here is also illustrative of a form of osteogenesis imperfecta which is not generally recognized, *i.e.*, osteoporosis without the markedly thinned cortices and slender shafts of the classic form. There is a great variation in the reported histologic findings in osteogenesis imperfecta, and this form of the disease does not resemble pathologically the infantile type. In view of the clinical findings, however, and the family history of brittle bones, blue sclerae, and deafness, our case, we believe, can with little doubt be placed in the osteogenesis imperfecta group. It is entirely possible that, on further investigation, some essential difference in underlying mechanism may be found, permitting separation of this form of the disease from the more commonly recognized classic type. In the meantime, the existence of this form must be borne in mind in the differential diagnosis of osteoporosis in young people.

SUMMARY

An unusual case of osteogenesis imperfecta in a twenty-eight-year-old woman has been reported. This patient exhibited multiple fractures, diffuse thickening of the calvarium, and marked osteoporosis. It is pointed out that calvarial thickening does not exclude a diagnosis of osteogenesis imperfecta. The case is also illustrative of a type of osteogenesis imperfecta characterized only by osteoporosis, without the thinned cortices and slender shafts of the classical form.

ACKNOWLEDGMENT: The author expresses his appreciation to the Department of Surgery of the University of Missouri School of Medicine for the clinical material used in this study.

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REFERENCES

1. BAKWIN, H., AND EIGER, M. S.: Fragile Bones and Macrocranium. J. Pediat. **49**: 558–564, November 1956.
2. CAFFEY, J.: Pediatric X-Ray Diagnosis. Chicago, The Year Book Publishers, Inc., 3rd ed., 1956.
3. FAIRBANK, T.: An Atlas of General Affections of the Skeleton. Edinburgh, E. & S. Livingstone, Ltd.; Baltimore, Williams & Wilkins Co., 1951.

SUMMARIO IN INTERLINGUA

Spissification Diffuse del Calvario in Osteogenese Imperfecte

Es reportate un caso de osteogenese imperfecte in un femina de vinti-octo annos de etate con un historia de repetite fracturas, scleras blau, difficultates auditori, e osteoporosis generalisate. Le patre e duo fratres senior suffreva de "ossos molle," con numerose fracturas, scleras blau, e defectos auditori. Contrari al presentia usual de subdisveloppamento cranial in iste morbo, le calvario del patiente esseva diffusemente spissificate. Ben que iste constatation es rar, le opinion es formulate que illo non exclude le diagnose de osteogenese imperfecte. Le caso differeva ab le forma classic del morbo etiam in le facto que le osteoporosis non esseva associate con marcate grados de tenuification del cortices e con diaphyses exigue.

Recurrent Gastric Ulcer Incident to Cortisone Therapy[1]

JAMES E. VICKERS, M.D.

WHILE THE occurrence of peptic ulceration of the stomach or duodenum due to adrenocortical preparations may be controversial, many reports in the literature would seem to substantiate the possibility. In the case to be reported here a very large gastric ulcer developed during cortisone therapy and promptly healed upon discontinuance of the drug. The ulcer recurred upon resumption of cortisone, but again healed when the medication was stopped.

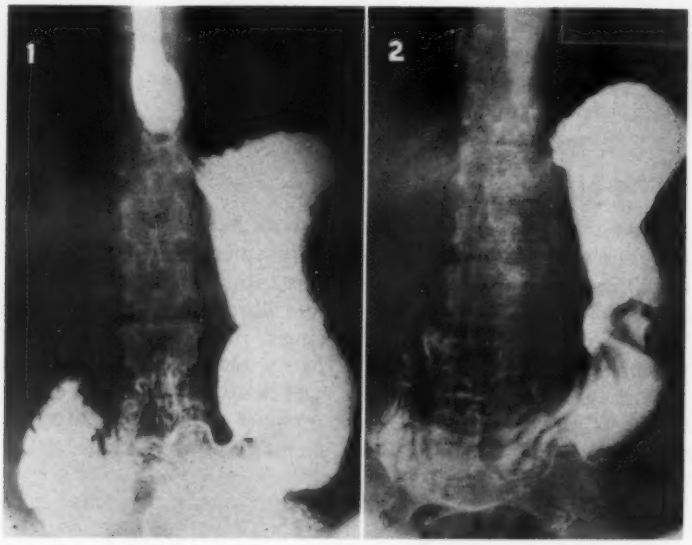

Fig. 1. April 2, 1956. Ulcer (5 cm.) on lesser curvature of stomach after prolonged cortisone therapy. An examination on Oct. 27, 1954, has been reported normal.

Fig. 2. April 16, 1956. Marked reduction in size of ulcer, five days after termination of cortisone.

CASE REPORT

A 62-year-old woman with angina and evidence of coronary insufficiency complained of severe pain in the left shoulder. This was treated with cortisone, 25 mg. three times daily, starting Nov. 17, 1953. The pain was moderately relieved and the drug was maintained. After three months, attempts to reduce the dosage were followed by a return of symptoms. Eleven months after the institution of cortisone therapy, on Oct. 27, 1954, a gastrointestinal examination, performed elsewhere, revealed no abnormal conditions.

In February 1956, the patient complained of epigastric distress and weakness. On March 28, 1956, she was hospitalized. The red blood cell count was 2,740,000, hemoglobin, 86 gm. Roentgen examination, April 2, disclosed a large gastric ulcer (Fig. 1). Treatment consisted of an ulcer diet, antacids, and transfusions. Cortisone was at first reduced to 25 mg. every other day and then discontinued, April 11. A repeat examination of the upper gastrointestinal tract on April 16 showed a marked reduction in the size of the ulcer (Fig. 2). The gastrointestinal symptoms completely subsided and another examination, May 17, showed the ulcer to be healed (Fig. 3).

In September 1956, the patient's only complaint was a recurrence of shoulder pain. Prednisone, 0.75 mg., one tablet three times daily, produced a slight

[1] From the Department of Radiology, University of Southern California, Los Angeles, Calif. Accepted for publication in February 1957.

relief of symptoms, and on Sept. 11, 14, and 18, 100 mg. of cortisone were given intramuscularly. Each injection brought about complete relief of symptoms for twenty-four hours.

On Sept. 26, pain in the abdomen again brought the patient to the hospital. A gastrointestinal examination disclosed a small gastric ulcer (1 cm. in diameter) at the site of the previous ulcer (Fig. 4). The cortisone was again stopped, whereupon the abdominal distress quickly subsided. A repeat examination on Nov. 8, 1956, revealed no evidence of ulcer (Fig. 5).

Fig. 3. May 17, 1956. Ulcer healed.

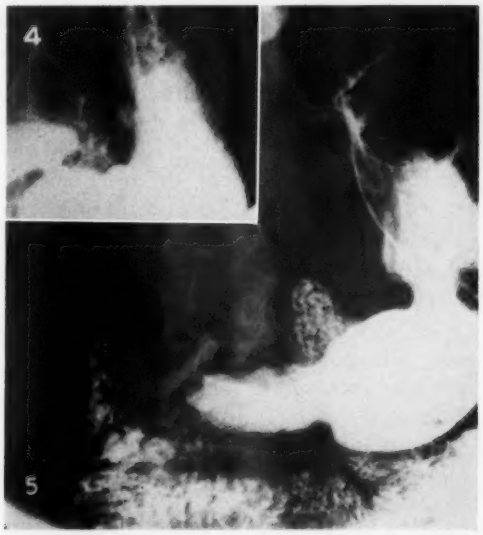

Fig. 4. Sept. 26, 1956. Small gastric ulcer on the lesser curvature of the stomach nineteen days after resumption of prednisone and cortisone.

Fig. 5. Nov. 8, 1956. Ulcer healed, thirty-two days after termination of adrenocortical medication.

DISCUSSION

Bollet *et al.* reported 3 cases of duodenal ulcer developing in patients under treatment with adrenocortical preparations (1). Among 141 arthritic patients receiving prolonged therapy with prednisone and prednisolone (2), Boland discovered 9 peptic ulcers.

Hirschowitz *et al.* administered corticotropin experimentally to 6 students. In 1 of these, with a previous history of peptic ulcer, roentgen evidence of an acute exacerbation developed (3). Brick is doubtful that any specific type of steroid therapy has a greater ulcerogenic property than another, or that the incidence of peptic ulcer is significantly increased in patients receiving adreno-cortical preparations (4).

It would seem, in the case presented here, that cortisone therapy was definitely related to the development of gastric ulcer. At the time of writing, further bleeding or gastrointestinal complaints had not been reported. Additional adrenocortical preparation therapy for this patient is not contemplated.

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REFERENCES

1. BOLLET, A. J., BLACK, R., AND BUNIM, J. J.: Major Undesirable Side-Effects Resulting from Prednisolone and Prednisone. J.A.M.A. **158:** 459–463, June 11, 1955.

2. BOLAND, E. W.: Prednisone and Prednisolone Therapy in Rheumatoid Arthritis; Clinical Evaluation Based on Continuous Observations for Periods of Six to Nine Months. J.A.M.A. **160:** 613–621, Feb. 25, 1956.

3. HIRSCHOWITZ, B. I., STREETEN, D. H. P., POLLARD, H. M., AND BOLDT, H. A., JR.: Role of Gastric Secretions in Activation of Peptic Ulcers by Corticotropin (ACTH). J.A.M.A. **158:** 27–32, May 7, 1955.

4. BRICK, I. B.: Drugs for Arthritis. J.A.M.A. **160:** 1168, March 31, 1956. Comment on Boland's article (2).

(*Pro le summario in interlingua, vider le pagina sequente*)

SUMMARIO IN INTERLINGUA

Recurrente Ulceres Gastric, Incidente a Therapia con Cortisona

Durante que le occurrentia de ulceration peptic del stomacho o del duodeno como effecto de preparatos adrenocortical es controverse, un numero de previemente reportate casos pare supportar un tal possibilitate. Es hic reportate un caso in que un grande ulcere gastric se disveloppava durante un curso de tractamento a cortisona dolores spatular. Le ulcere dispareva post le interruption del uso del droga. Illo se disveloppava de novo quando le curso de cortisona esseva reinstituite e dispareva de novo quando le tractamento esseva interrumpite de novo.

Rapid Osseous Changes in Syringomyelia[1]

GEORGE A. MEYER, M.D.,[2] JOSEPH STEIN, M.D.,[3] and MAXWELL H. POPPEL, M.D.[4]

THE ROENTGEN manifestations of neuropathic arthropathies are well known (1–4). The correlation between the onset of disease and significant roentgen changes, however, is not clear and deserves further consideration.

Cases of syringomyelia have been described (7, 8) in which joint changes developed within a relatively short time, yet the exact mechanism was not always satisfactorily established.

PATHOGENESIS AND PATHOLOGY

Several theories (9) have been advocated to explain the pathogenesis of syringomyelia: (*a*) that cavities arise in gliotic tissue within ependymal cell rests; (*b*) that the condition is a developmental anomaly related to imperfect formation of the central canal, which, however, does not explain the frequent finding of cavities in the dorsal part of the posterior horn, where ependymal cells are never found; (*c*) that the significant factor is the presence of intramedullary vascular anomalies (9). Vascular hemorrhage and occlusion, with a concomitant alteration of blood flow, would account for an initially rapid onset of symptoms and subsequent slow quiescence and/or progressive disease. In addition, the cervical and lumbar regions are best vascularized, and they are most often the site of the disease.

Neuropathic arthropathies occur as the result of repeated injuries to articulations in which sensory perception is diminished. The following changes are seen (5, 10): enlargement of the joint due to effusion; relaxation of the ligaments with subsequent instability and deformity; thinning of articular cartilage; marginal fractures; condensation of subchondral bones; loose bodies in the joints; formation of new bone outside the joint cavity. Any process damaging proprioception of joint structure will lead to traumatic changes. When the protective sensory innervation has been diminished, minor trauma is not recognized. Continued damage to the joint with extensive injury of the articular cartilage and subchondral bone eventually will result in disintegration of the cartilage and articular surface. Clinically, arthropathies develop in 25 per cent of cases of syringomyelia, and 80 per cent of syringomyelia arthropathies involve the upper extremities. The initial symptomatology is referable to swelling of the joint and limitation of motion.

DISCUSSION

Ninety per cent of neuropathic arthropathies are related to tabes dorsalis, while the remaining 10 per cent are due principally to syringomyelia. Charcot observed that joint changes occurred following damage to "trophic centers" in the spinal cord or following degeneration of peripheral nerves.

In 1917, Eloesser (6) demonstrated the role of trauma in neuropathic joint changes, on the basis of animal experiments. Following section of the posterior roots alone, no changes in the joints took place but, after section of the posterior roots with concomitant trauma, development of neuropathic arthropathies ensued. Thus the concept was derived that continued function in an analgesic joint with resulting trauma would lead to arthropathies. Fur-

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thermore, it was assumed that the greater the activity occurring in such a joint, the more rapidly would the arthropathies set in. This would explain the more rapid change in lower extremities where weight-bearing occurs, as compared to the upper extremities, which are under less stress.

In an analysis (7) of 7 cases of neuropathic arthropathies due to syringomyelia, seen in a Danish hospital, there was noted a slow development of anesthesia and muscular atrophy of the upper extremities. In the early stage, soft-tissue swelling was noted with no osseous changes visible roentgenographically. In the intermediate stage, destruction of the joint took place, with calcification in the soft tissues. In a late stage, progressive atrophy and absorption of bone were noted. In 5 patients from this series, extensive bone destruction developed in a period of five to twelve months, and in 1 patient extensive bone destruction occurred after three months.

The concept of a painless joint destroyed by excessive wear due to loss of sensory perception was questioned in the foregoing report. It was pointed out (*a*) that the affected joints are painful in half the cases of syringomyelia and (*b*) that joint destruction may develop rapidly without any preceding trauma. To explain this, one may assume a progressive process in the spinal cord resulting in vascular changes in and around the joint with subsequent development of neuropathic arthropathies.

Pendergrass (8) described a case of syringomyelia with rapid joint changes in which clinical evidence of joint destruction occurred in three weeks, with roentgen evidence in five weeks. In the case which follows, significant roentgen changes occurred between Sept. 9 and Nov. 19, 1952, with absorption of major parts of the anatomical neck of the right humerus.

The explanation of the rapid onset of neuropathic osseous changes lies in the factors mentioned above, since trauma and absence of pain have not been observed in all cases. A progressive process in the spinal cord, with vascular changes, would appear to be a more plausible explanation.

CASE REPORT

A 37-year-old colored male was admitted to the hospital on Aug. 19, 1952, complaining of numbness of the right upper extremity of four months duration. The "numbness" extended also to the right side of the neck and the right occipital and post-auricular area. Moreover, there had been present a sensation of "pins and needles" in the right hand for several months.

The patient had apparently enjoyed good health until three or four months prior to admission, when he first noticed the numbness of the right arm and the sensation of "pins and needles" in the hand. His earlier medical history was not remarkable.

On physical examination, the patient appeared in no distress and the findings were not remarkable, except for the following neurological features: hypesthesia and hypalgesia; diminished temperature sensation in the area supplied by the dermatomes C-2 through C-8; areflexia in the right upper extremity; weakness of the deltoid and biceps on the right, with some atrophy of the right biceps brachialis; diminished stereognosis. On the basis of these findings, a lesion in the cervical cord involving the spinal segments C-2 through C-8 was considered.

The process was localized in the spinothalamic tracts and/or the anterior commissure, leading to a loss of pain and temperature sensation in the right upper extremity. There was also involvement of the dorsal column, leading to touch, position, vibratory and stereognostic loss in the right upper extremity. That there was encroachment upon the anterior horn cells was shown by weakness of the right deltoid and right biceps brachialis, along with atrophy of the right biceps.

Roentgenograms of the right shoulder dated Sept. 9, 1952 (Fig. 1) demonstrated erosive changes involving the greater tuberosity of the humerus and the outer end of the acromial process. These findings were considered to be compatible with secondary changes due to repeated trauma, and the possibility of chronic recurrent dislocation was mentioned. Electromyography revealed no presence of fibrillations.

The patient was discharged on Sept. 26, 1952, and referred to the follow-up clinic. On Nov. 18, he was readmitted, complaining of progressive pain along the anterior aspect of the right shoulder, sharp and constant, of several weeks duration.

Physical examination at this time revealed a large swelling about the shoulder with tenderness over the distal tip of the clavicle. Crepitation and limited motion were observed. Abduction to 45° was possible. Sensation was diminished along the posterior aspect of the shoulder joint, as well as on the lateral aspect of the arm and forearm. There was also noted decreased sensation along the arm and forearm. In addition, there was loss of temperature sensation of the right arm.

Radiographic examination of the right shoulder

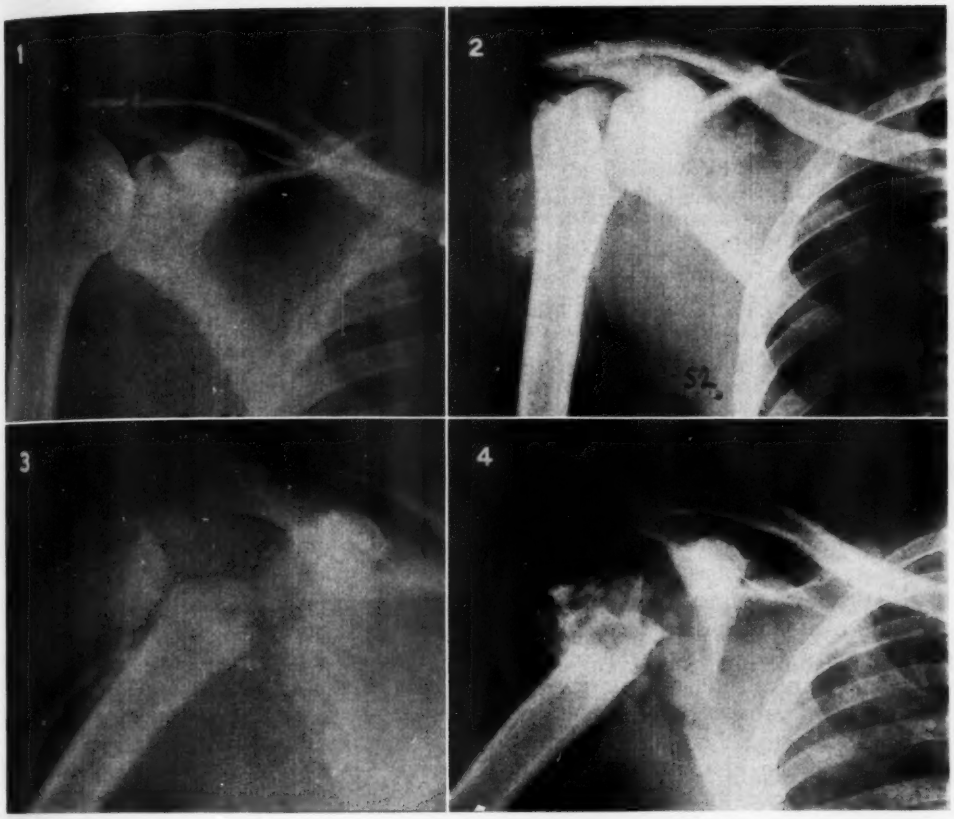

Fig. 1. Sept. 9, 1952. Minimal erosive changes involving the greater tuberosity of the right humerus and the outer end of the acromial process.

Fig. 2. Nov. 19, 1952. Absorption of the major portion of the anatomical neck of the right humerus. There remains only a small part of the articular portion of the humeral head. Note large amount of calcification in the soft tissues of the shoulder joint.

Fig. 3. Jan. 28, 1953. Extensive absorption of the neck and head of the humerus. Soft-tissue calcification and periosteal proliferation along the upper end of the humerus.

Fig. 4. Dec. 19, 1954. Disorganization of the head of the right humerus and the glenoid process of the scapula. Extensive fragmentation of bone into the soft tissues and some eburnation of the adjacent bone surfaces.

Nov. 19, 1952 (Fig. 2) showed absorption of the major portion of the anatomical neck of the right humerus. There still remained a small part of the articular portion of the humeral head. In addition, there were noted a large amount of calcification in the soft tissues of the shoulder joint, a lucent area in the upper portion of the greater tuberosity, and a moderate degree of periosteal proliferation on the upper medial aspect of the humerus.

Roentgenograms obtained on Jan. 28, 1953 (Fig. 3), again showed the presence of a neurotrophic joint on the right, with extensive soft-tissue calcification and periosteal proliferation along the upper end of the humerus. Also there were seen a small lytic notching of the lateral aspect of the acromial process and a moderate subluxation of the remaining portion of the humerus in relation to the glenoid fossa.

Examination of the shoulder Dec. 19, 1954, showed disorganization of the head of the humerus and the glenoid process of the scapula. There were extensive proliferation of bone into the soft tissues and some degree of eburnation of the adjacent bone surfaces. This represents an advance of the process, particularly in respect to proliferation and fragmentation, since the examination of January 1953.

The significant features of this case of syringomyelia are the short interval—less than two and a half months—between a radiographic study demonstrating only a minimal degree of erosive change involving the greater tuberosity of the humerus (Sept. 9, 1952) and an examination showing ab-

sorption of the major portion of the anatomical neck of the humerus (Nov. 19, 1952).

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REFERENCES

1. PUGH, D. G.: Roentgenologic Diagnosis of Diseases of Bones. Reprinted from Nelson's Loose-Leaf Diagnostic Roentgenology. Baltimore, Md., Williams & Wilkins Co., 1952.

2. LUCK, V. J.: Bone and Joint Diseases. Springfield, Ill., Charles C Thomas, 1950.

3. BRAILSFORD, J. F.: Radiology of the Bones and Joints. Baltimore, Md., Williams & Wilkins Co., 4th ed., 1948.

4. RITVO, M.: Bone and Joint X-ray Diagnosis. Philadelphia, Penna., Lea & Febiger, 1955.

5. SOTO-HALL, R., and HALDEMAN, K. O.: The Diagnosis of Neuropathic Joint Disease (Charcot Joint); Analysis of 40 Cases. J.A.M.A. **114:** 2076-2078, May 25, 1940.

6. ELOESSER, L.: On the Nature of Neuropathic Affections of the Joints. Ann. Surg. **66:** 201-207, August 1917.

7. SKALL-JENSEN, J.: Osteoarthropathy in Syringomyelia. Analysis of Seven Cases. Acta radiol. **38:** 382-388, November 1952.

8. PENDERGRASS, E. P., GAMMON, G. D., AND POWELL, J. H.: Rapid Development of Bone Changes in a Patient with Syringomyelia as Observed Roentgenologically. Radiology **45:** 138-146, August 1945.

9. NETSKY, M. G.: Syringomyelia: A Clinicopathologic Study. Arch. Neurol. & Psychiat. **70:** 741-777, December 1953.

10. SHANDS, A. R., JR.: Neuropathies of Bones and Joints. Report of Case of Arthropathy of Ankle Due to Peripheral Nerve Lesion. Arch. Surg. **20:** 614-636, April 1930.

SUMMARIO IN INTERLINGUA

Rapide Alterationes Ossee in Syringomyelia

Es reportate un caso de syringomyelia con extense alterationes ossee disveloppate in le articulation humeral intra un periodo de minus que duo menses e medie. Roentgenogrammas facite le 9 de septembre 1952 demonstrava solmente minime grados de alteration erosive in le tuberositate major del humero. Le 19 de novembre del mesme anno, un restudio monstrava un extense disorganisation del capite humeral e del portion glenoide del scapula, fragmentation del osso a in le histos molle, e un certe eburnation del adjacente superficies ossee.

Le affection articular in iste e simile casos es attribuite a un processo progressive in le medulla spinal con alterationes vascular in e circa le articulation.

Extended Range Radiography

Preliminary Report[1]

GERHART S. SCHWARZ, M.D.

THE MOST SERIOUS deficiency of present-day radiography is its narrow subject range. To date it is impossible to view on a radiograph, simultaneously, thin and thick or opaque and radiolucent parts of the patient's body because the human eye cannot utilize the dark portions of the film. For instance, when the spine is adequately exposed on a radiograph of the thorax, the ribs are lost in the dark areas and soft-tissue detail is so completely obliterated that it cannot be recognized even under a bright spotlight.

Wherever the density of the film exceeds 2.5, some information recorded on it is lost to the observer because the reading of radiographs is a process of direct transparency viewing and therefore limited by the physiology of the human eye. Raising the illumination level of a standard viewbox is of no avail since it brightens the transparent areas of the film excessively. This blinds the observer so that the reading of the dark film areas is even more unsatisfactory. The present standard viewbox possesses the optimum degree of illumination, and this should not be changed. The use of a bright spotlight with narrow shutters or a small diaphragm helps but converts film reading into a process of scanning which reduces simultaneous visual information to sequential information. This is undesirable. Moreover, there is loss of definition in the dark areas of the film when they are penetrated by a bright spotlight because of diffusion of light passing through a thick layer of silver granules. This produces a blotting-paper effect.

One of the solutions to this problem lies in the manufacture of x-ray fi'm with very thin emulsions, so that its maximum density can be limited to 2.5–2.8.[2] The first practical step in this direction was taken by Mr. James Melton, R.T., who demonstrated to us that single-coated film possesses an increased subject range in medical radiography and tolerates over-exposure well because of its low silver content. We have now used blue sensitive single-coated Eastman Kodak antihalation-backed x-ray film for six months and have found it capable of extending subject range. This film is commercially available through regular channels. Similar products of two other manufacturers were eliminated, for the time being, after brief testing, one because of fogging, the other because of too high a silver content.

The antihalation backing of both films is completely opaque. Single-coated film of this type can be placed in any conventional double-screen cassette with its emulsion facing either the front screen or the back screen and will receive light from only that screen which it faces. This reduces the speed of the film so that one must increase

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[1] From the Department of Radiology, College of Physicians and Surgeons, Columbia University, and the Radiological Service of the Presbyterian Hospital, New York City. Accepted for publication in March 1957.

[2] The densitometric explanation of the problem is as follows: The density range which the eye can utilize simultaneously without strain when viewing transparencies extends approximately from 0.2 to 2.7 and represents a density scale of 2.5 (2.7 minus 0.2). Conventional double-coated x-ray film, however, possesses a maximum density of 3.2, and special high-kv x-ray film the even higher maximum density of 4.5. When the subject range which is recorded on the film is spread over a density range of 0.2 to 3.2, or more, a portion of it is lost to the observer. In order to transmit all of the recorded subject range to the viewer, it is necessary to compress it into the useful density scale of 2.5. This can be achieved by limiting the silver content of the emulsion, *i.e.*, by reducing its thickness. The optimum is reached when the transmitted subject range equals the recorded one. This produces the maximum utilization of the recorded subject range.

Not every thin emulsion produces the desired effect. Emulsions in common use twenty to thirty-five years ago, though thin, lacked a sufficiently wide exposure scale and were incapable of recording a wide subject range because their characteristic curve was too steep, *i.e.*, possessed too high a gamma. Present-day emulsions—because they are more sensitive—possess a lower gamma at the same thickness and make it possible therefore to record a wide subject range without requiring high negative densities.

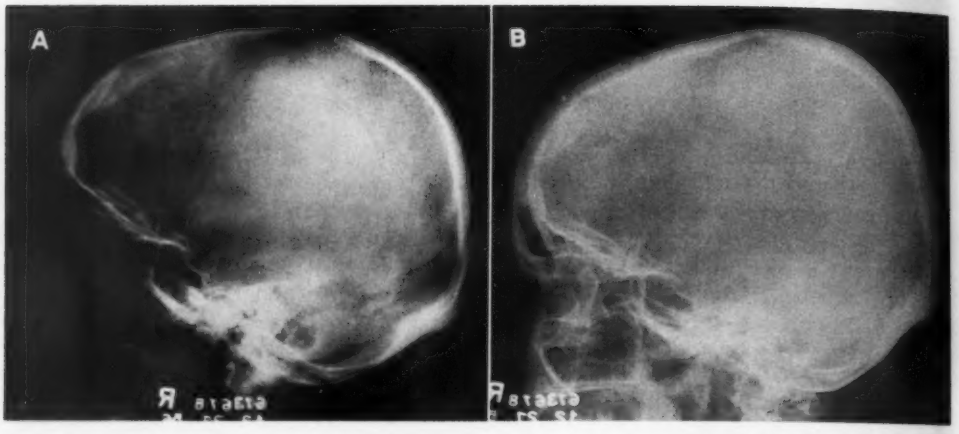

Fig. 1. Comparison of double-coated and single-coated film, to illustrate difference in subject range.
A. Lateral roentgenogram of skull on double-coated film in double-screen cassette (par-speed), 76 kv, 32 mas. The calvarium is correctly exposed and well demonstrated. The facial bones and skin cannot be recognized adequately.
B. Lateral roentgenogram of same skull on single-coated film in monoscreen cassette (no front screen; par-speed), with same exposure factor as in A. Skin, subcutaneous tissues, facial bones, as well as the calvarium, are visualized diagnostically.

the milliampere seconds by about 60 to 100 per cent or the kilovoltage by 10 to 15 per cent. One can remove the front screen of the cassette, however, when the single-coated film is inserted with its emulsion facing the back screen. This eliminates from the cassette an absorbing layer of material which is no longer needed. Such a combination of monoscreen cassette and single-coated film requires only a 30 to 50 per cent increase of milliampere seconds over the conventional combination of double-screen cassette and double-coated film. If the antihalation backing was removed chemically before use, it became possible to utilize the light of both screens of the conventional cassette. "Clear-back" single-coated film exposed in this manner has almost speed parity with double-coated Blue Brand film at voltages up to 85 kv, *i.e.*, the loss of speed is small enough to permit the same exposure settings for both films.

Double-coated film has also been tried in monoscreen cassettes and in cassettes in which one screen was covered with black or yellow opaque paper. The results were inferior because the unused emulsion facing the covered screen produced an image also, through exposure to x-rays and to light transmitted through the front emulsion. This could be proved by alternately scraping one or the other emulsion from the film base.

The subject range of the single-coated film tested is sufficiently wide to permit the simultaneous viewing of skin, subcutaneous tissues, nasal bones and calvarium on a lateral radiograph of the skull without loss of diagnostic detail. A lateral view of the spine depicts the thoracic and the lumbar section diagnostically on a single film. In placentography it has been found useful for the taking of the lateral view with and without the use of a wedge filter.

There are two disadvantages to this system: Loss of contrast and loss of speed. Loss of film speed could be overcome by manufacture of a double-coated film of lower silver content or a single-coated film with a transparent back. This makes it possible to utilize both screens of the cassette and yet retain the advantage of extended radiographic range. Negotiations with manufacturers are in progress. Use of Auer-Flash screens has enabled us to increase the speed of single-coated film to twice that of double-coated film when used with two par-speed screens, so that the

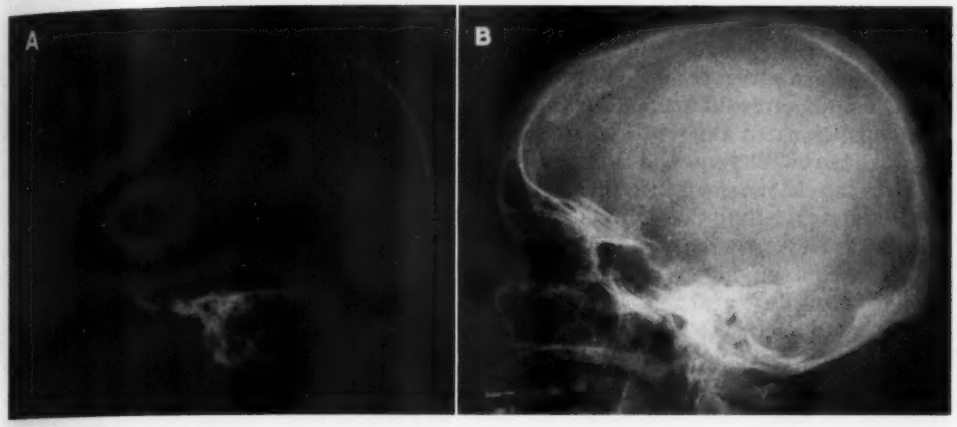

Fig. 2. Tolerance to over-exposure. Over-exposed radiographs of the skull of the same patient whose normally exposed films are shown in Fig. 1. The same kilovoltage, distance, and grid were used for all four exposures. The only factor varied was the milliampere seconds.

A. Double-coated film in double-screen cassette (par-speed); twice normal exposure; 76 kv, 64 mas. The radiograph is too dark and is diagnostically unacceptable.

B. Single-coated film in monoscreen cassette (par-speed) given a fourfold over-exposure; 76 kv, 128 mas. The radiograph, though dark, is still diagnostic.

patient exposure is less now for single-coated film technic than for our conventional technic. Eventually, however, the advantages of Auer screens will be applied to the conventional technic also, so that this point of superiority is a temporary one.

As a rule, we have not found the loss of contrast objectionable except in chest work. In pyelography and cholecystography selective iodine contrast is preserved on single-coated film. It is rarely used for this purpose, however. Our use of single-coated film is confined at present to radiography of the pelvis, spine, placenta, skull, ribs, and extremities. In distal extremity work, we now use single-coated film in cardboard holders often in lieu of standard double-coated non-screen film. This requires increasing the milliampere seconds two and a half times

The contrast problem could be overcome in part by applying two different emulsions to the aforementioned special double-coated film. By using a narrow-range, high-contrast, low-threshold emulsion on one side of the film base and a low-contrast emulsion of high threshold on its opposite surface, one can obtain high contrast in a limited range and a general low contrast in the rest of the range. Attempts at introducing color as an additional discriminatory agent have been made by others in an effort to increase range without loss of contrast. At present, both methods are impractical because they lower film speed, or require additional processing, and often necessitate multiple exposures. The use of color pigments in lieu of silver granules has the additional advantage, however, of reducing internal diffusion for viewing and projecting.

Until a special emulsion becomes commercially available, this department will continue the use of single-coated film. At present, about 10 per cent of all our routine films taken are single-coated. We anticipate a rise to about 30 per cent as soon as an adequate number of monoscreen cassettes is received. Lack of these cassettes has prevented us from using this system more extensively to date. The method has been found to be superior to high-kilovoltage technic in that it reduces contrast without loss of differential absorption. The following secondary advantages were observed: high tolerance to over-exposure, improved photographic reproductions without LogEtronics, and a slight increase in resolution of bone detail.

Historically the method may seem to

constitute a return to the old single-coated glass plate. In practice this is not the case. Modern advances in emulsion and screen manufacture have made it possible to use single-coated film without any major disadvantage. The method is contraindicated when a narrow-range coned-down spot view is to be obtained, because maximum contrast is then the primary objective.

The accompanying reproductions are intended to illustrate the advantage of single-coated over double-coated x-ray film. Photographic reproductions tend to minimize the difference between the two methods so that the illustrations do not adequately portray the superiority of single-coated film.

SUMMARY

It is possible to extend the transmitted subject range of modern radiographs to equal the recorded subject range, thereby making possible maximum utilization of recorded information. This is accomplished by reducing the silver content of the emulsion of the film so that its density scale is limited to approximately 2.5. This represents the optimum adaptation of radiographs to the optic physiology of direct transparency viewing as far as subject range is concerned.

A partial technical solution consists of the use of single-coated x-ray film. Six months experience with the use of a commercially available film of that type is reported. An extended radiographic range and a high tolerance to over-exposure were observed. A moderate loss of contrast and speed were encountered but it was felt that the advantage of extended range outweighed these deficiencies in certain radiographic applications. They can be overcome by technological modifications, which are discussed briefly.

NOTE: To make clear the use of certain terms employed in this paper, the following list of definitions is included:

Density: Logarithm of $\frac{\text{intensity of incident light}}{\text{intensity of transmitted light.}}$

Density of emulsion: Density of any given point on a film possessing a given emulsion after exposure and normal development.

Density range: Lowest and highest density a film can attain after normal development, as a result of exposure.

Density scale: Highest density minus lowest density, as defined above.

Useful density scale: That portion of the density scale which can be utilized by the eye of the observer when viewing a transparency directly.

Recorded subject range: (= exposure scale): Smallest amount and largest amount of exposure capable of increasing the density of the emulsion, *i.e.*, capable of being recorded on the film.

Transmitted subject range: That portion of the recorded subject range which can be utilized by the human eye, *i.e.*, is transmitted to the observer directly without auxiliary devices such as spotlights, photographic prints, video scanners, electronic contour enhancers, or LogEtronic reproductions.

Characteristic curve: Graphic demonstration of emulsion density as function of the logarithm of exposure.

Gamma: Tangent of the maximum angle of the slope of the characteristic curve after normal development.

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SUMMARIO IN INTERLINGUA

Meliorate Inclusivitate Radiographic: Reporto Preliminar

Il es possibile augmentar le transmittentia del moderne pellicula radiographic de maniera que le inclusivitate thematic que es transmittite equala le inclusivitate thematic que es registrate. Assi on pote obtener un utilisation maximal del information registrate. Isto es effectuate per reducer le contento de argento in le emulsion del pellicula de maniera que su grado de densitate es restringite a approximativemente 2,5. Sub iste conditiones on obtene le optime adaptation del pellicula radiographic al physiologia optic del examine directe de transparentias con respecto al inclusivitate thematic.

Un partial solution technic del problema consiste in le uso de pelliculas roentgenographic a solmente un revestimento de

emulsion. Es reportate le experientias in le uso, durante sex menses, de un commercialmente obtenibile pellicula de ille genere. Un augmento del inclusivitate thematic del radiographias e un alte grado de tolerantia pro hyperexpositiones esseva constatate. Un moderate perdita de contrasto e de velocitate esseva incontrate, sed il pareva que le avantage del augmentate inclusivitate esseva plus que un compensation de iste imperfectiones. In plus, le imperfectiones in question pote esser eliminate per modificationes technologic, le quales es discutite brevemente.

Al tempore del presente reporto, le uso de pelliculas a un revestimento es restringite al radiographia del pelve (obstetric e orthopedic), del columna vertebral, del placenta, del cranio, del costas, e del extremitates.

EDITORIAL

Clinical Management of the Patient with Advanced Cancer

Management of the patient with advanced cancer is as much a clinical art as a scientific process. Such professional assignment requires of the radiotherapist, as of all physicians, dedication to the personal welfare of the patient and a broad understanding of the course of cancer, its symptomatology, and the potential roles of surgery, irradiation, medication, and philosophy in management. In this issue of RADIOLOGY, a symposium on advanced cancer is presented by a general surgeon, a radiologist, a regional specialist, and an internist.[1] As Dr. Grantley Taylor advises, it is best that one physician accept the overall responsibility of managing the patient and dealing with the family, even though the combined efforts of a team of experts may be needed to provide various diagnostic and therapeutic procedures contributing to total care.

At the outset it is essential to evaluate critically whether or not the patient really has incurable cancer. Occasionally secondary inflammation or post-irradiation necrosis masquerades as advanced cancer. Some lesions considered incurable ten years ago can now be brought under control by the more extensive surgical resections of today, by more effective radiotherapy, or by advantageous combinations of radiotherapy and surgery. The effectiveness of radiotherapy has been increased through better physical control of dosage, more versatile technics, and more potent facilities permitting delivery of prescribed dosage to the tumor with reduced irradiation of uninvolved tissues. A patient with cancer of questionable incurability should be reviewed by both a surgical and radiotherapeutic consultant before the disease is pronounced beyond possible control and treatment is restricted merely to palliation. It is a serious error to fall short of adequate treatment for extensive but still controllable disease. When cancer has been established as incurable, crippling surgery or necrotizing radiotherapy is not justified; palliation then becomes the ultimate goal.

The purpose of palliative therapy is to provide relief of distress from disease and to prolong the period of enjoyable and useful life. Whether it be by surgery, irradiation, or drugs, palliative treatment should be planned and purposeful, as emphasized by Dr. Milford Schulz in his presentation in this symposium. Formulation of the therapeutic program should be based on analysis of the particular problem of the individual patient, with due consideration of the resectability, radioresponsiveness, endocrine dependence, and the extent and general nature of the disease. Treatment should offer some promise for alleviation of pain, relief of obstruction, control of hemorrhage, reduction of malodorous discharge and infection, lessening of deformity, improvement in certain bodily functions, or benefit of general health. Major therapy should not be undertaken just to satisfy the urge of the oppressed referring physician or the demands of an agitated family, insisting that "something must be done." Such a situation is at times best met by frank discussion with the family, professional composure, and good personal care of the patient. Dr. Herbert Schmitz urges that the plight of the incurable patient should never be considered hopeless, since the maintenance of intelligent interest in him and his problems fosters

[1] See pages 321–346.

courage, comfort, and true benefit of intangible value.

Endocrine therapy has contributed remarkable palliation in some cases of advanced cancer of the prostate and cancer of the breast. The roles of deprivation and addition of estrin, of testosterone therapy, and of adrenalectomy and hypophysectomy in advanced mammary cancer have been reviewed by Dr. B. J. Kennedy in this symposium.

Chemotherapy by cytotoxic agents and metabolic antagonists is currently receiving wide publicity and enthusiastic experimental application in advanced cancer. Although no long-range survivals or cures of any neoplastic disorder have been achieved by this means, it does offer a therapeutic modality applicable to certain leukemias, lymphomas, lung cancers, and various preterminal neoplasms. Chemotherapeutic agents are not innocuous, since all carry the hazards of suppression of hematopoiesis, with anemia, leukopenia, and hemorrhagic states.

Management of the patient with advanced cancer involves also protection of the family and patient against invasion of their hope and credulity by dishonest quacks and false prophets with distorted proclamations. Zealous press reports of astounding cancer cures evolving from centers of learning, philanthropic organizations, and governmental agencies, though released in the spirit of enlightenment and in justification for continued support, frequently kindle false hopes of cure from the advertised marvel and arouse dissatisfaction with established therapy in patients with incurable disease. It therefore behooves the physician and consultant to the cancer patient to keep abreast of current developments in cancer research in order that he may better evaluate the recurring claims for newer and better "cancer cures" and then discuss authoritatively the background and validity of such claims with the inquiring family and distraught patient.

HOWARD B. HUNT, M.D.

IN MEMORIAM

IRA HIRAM LOCKWOOD, M.D.

1885–1957

It is with considerable misgiving that I undertake to write this obituary for our friend and colleague, Ira Hiram Lockwood. I fear that my words are inadequate to express the measure of his life and achievements or the esteem of his friends and colleagues. Life began for Ira Nov. 29, 1885, in Storm Lake, Iowa. There he obtained part of his schooling, graduating with a B.S. degree from Buena Vista

College, which also gave him the honorary degree of Doctor of Science in 1956. He attended Iowa University from 1905 to 1907 and was graduated in Medicine from General Medical College, Chicago, in 1909. There followed a few years of general practice in Lincoln, Nebr., and then World War I. In this conflict Dr. Lockwood held the rank of Major, first as Chief of the X-ray Department of Evacuation Hospital #1 AEF and later as head of the X-ray Service, 2nd Army AEF.

In 1924 Dr. Lockwood became associated with the late Dr. Edward Holman Skinner in Kansas City. He has since been Chief of Radiology at the Research Hospital and head of the Department of Radiology of Research Clinic, a venture largely accredited to him. He served as Chief of the Residency Training Program of Research, the Kansas City General Hospitals, Childrens Mercy, and the Veterans Administration Hospitals of Kansas City and Wadsworth. He was also Chief Consultant in Radiology for the Veterans Administration in Missouri, Kansas, Oklahoma, and Arkansas. These were his principal positions, but in addition he and his teams of younger radiologists made regular circuits of some of the towns around Kansas City, bringing better radiology to the smaller communities.

Locally Dr. Lockwood served as President of the Kansas City Southwest Clinical Society, Jackson County Medical Society, and as head of the Research Hospital and Research Clinic Staffs. Nationally he was a member of the Radiological Society of North America and American Roentgen Ray Society, and an Honorary Member of the American Radium Society. He served as President of the Radiological Society of North America in 1953 and Chairman of the Board of Chancellors and President of the American College of Radiology. The latter position he held at the time of his death.

Both the American College and the Radiological Society awarded him gold medals for his contributions to radiology. His activities, however, were not limited to that specialty. He was always in the forefront in civic activities and was especially active in the formation of the Blue Cross-Blue Shield Plans, both locally and nationally from their inception. He was one of our most active exponents of the idea that the medical profession itself should put good medicine within the reach of everyone. How well he and the many others who helped to institute these plans succeeded is attested by the present scope of the Plans themselves.

Dr. Lockwood's 81 published articles and many exhibits brought him several awards, including a Certificate of Merit from the Radiological Society of North America for a scientific exhibit on Breast Radiography. He was deeply interested in education, and to him many a young man owes his start in radiology. He was always seeking to improve the standards of medical practice, especially radiology. He became a Diplomate of the American Board of Radiology in 1934 and served, since the inception of the Board, as Trustee and later as President and Chairman of the Executive Committee. No one was more active in examining and helping the young radiologist who sought certification by the Board than he.

On Sunday, July 28, Dr. Lockwood died peacefully in his sleep, having survived his charming wife, Jessie, about two years. His was a life endowed with ample energy and the will and the spirit to contribute greatly in the service of mankind. He will be missed from our councils and by his host of friends.

C. EDGAR VIRDEN, M.D.

ANNOUNCEMENTS AND BOOK REVIEWS

THE AMERICAN BOARD OF RADIOLOGY

The American Board of Radiology has announced the election of the following officers: President, Dr. Donald S. Childs, Syracuse, N. Y.; Vice-President, Dr. B. P. Widmann, Philadelphia; Secretary, Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.; Treasurer, Dr. J. W. J. Carpender, Chicago. Members of the Board of Trustees are Dr. Robert Barden, Philadelphia; Dr. John D. Camp, Los Angeles: Dr. E. L. Jenkinson, Chicago; Dr. Traian Leucutia, Detroit; Dr. Ira H. Lockwood,* Kansas City, Mo.; Dr. F. W. O'Brien, Boston; Dr. Douglas Quick, New York; Dr. Leo G. Rigler, Los Angeles; Dr. Laurence L. Robbins, Boston; Dr. Ernest H. Wood, Chapel Hill, N. C.

The following are the latest requirements for examination for certification by the Board:

In Radiology: Those beginning their training *before* July 1, 1956, must have three years formal residency training in an approved department of radiology.

Those beginning their training on July 1, 1956, or thereafter must have three years formal residency training in an approved department of radiology plus an additional year of either further training or practice. The three-year training period must include the equivalent of six months (total) in pathology and isotopes.

Those beginning their training on July 1, 1956 or thereafter will be required to take a written examination in physics (including physics of isotopes) and pathology at the *completion* of their formal training. Acceptance for the oral examination is contingent upon passing the written examination. (The written examination in the above two mentioned phases of radiology will abolish the oral.)

In Diagnostic Roentgenology: Those beginning their training *before* July 1, 1956, must have two and one-half years formal residency training in an approved department of radiology. The equivalent of six months of this time must have been devoted to pathology.

Those beginning their training on July 1, 1956, must have two and one-half years formal residency training in an approved department of radiology (the equivalent of six months of which time must have been devoted to pathology) plus an additional year of either further training or practice.

Those beginning their training on July 1, 1956, or thereafter will be required to take a written examination in physics and pathology at the *completion* of their formal training. Acceptance for the oral examination is contingent upon passing the written examination. (The written examination in the above two mentioned phases of radiology will abolish the oral.)

Those beginning their training on July 1, 1957, or thereafter will be required to take three years formal residency training in an approved department of radiology, the first year of which must be spent in basic training (pathology, physics and basic radiologic technics), followed by two years clinical training. They will also be required to take an additional year of either further training or practice. (Written examination also required for these candidates. See above paragraph.)

In Therapeutic Radiology: Those beginning their training *before* July 1, 1956, must have two and one-half years formal residency training in an approved department of radiology. The equivalent of six months of this time must have been devoted to pathology.

Those beginning their training on July 1, 1956, must have two and one-half years formal residency training in an approved department of radiology (the equivalent of six months of which time must have been devoted to pathology) plus an additional year of either further training or practice.

Those beginning their training on July 1, 1956, or thereafter will be required to take a written examination in physics (including physics of isotopes) and pathology at the *completion* of their formal training. Acceptance for the oral examination is contingent upon passing the written examination. (The written examination in the above two mentioned phases of Radiology will abolish the oral.)

Those beginning their training on July 1, 1957, or thereafter will be required to take three years formal residency training in an approved department of radiology, the first year of which must be spent in basic training (pathology, physics, physics of isotopes and basic radiologic technics), followed by two years clinical training. They will also be required to take an additional year of either further training or practice. (Written examination also required for these candidates.)

Those applying for Therapeutic Radiology alone must show evidence of personal experience in the use of intracavitary and interstitial radium or equivalent sources, as well as proficiency in roentgen therapy.

Prior to July 1, 1960, those candidates desiring to be certified in either Radiology or Therapeutic Radiology, will be urged to take an examination in Nuclear Medicine. After July 1, 1960, this examination will be mandatory.

Those candidates previously certified in Roentgenology desiring to complete their certificate in Radiology (including Nuclear Medicine) will be required to have the equivalent of six months full-time radium and isotope training in an approved department of radiology.

Prior to July 1, 1960, those candidates who have been previously certified in Roentgenology and who

* Deceased.

do not desire to be examined in Nuclear Medicine must have the equivalent of three months full time radium training in an approved department of Radiology.

MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA SECTION ON RADIOLOGY

Forrest V. Schumacher, M.D., has recently been elected Chairman of the Section on Radiology of the Medical Society of the District of Columbia. Melvin O. Goodman, M.D., is Vice-Chairman; and Charles E. Bickham, Jr., M.D., 1835 Eye St., N. W., Washington 6, D.C., Secretary-Treasurer.

RADIOLOGICAL SOCIETY OF LOUISIANA

Newly elected officers of the Radiological Society of Louisiana are: President, M. Ragan Green, M.D., Ruston; Vice-President, J. T. Briere, M. D., New Orleans; and Secretary-Treasurer, Seymour Ochsner, M.D., Ochsner Clinic, New Orleans 15.

NASSAU RADIOLOGICAL SOCIETY

The Nassau Radiological Society (New York) recently elected the following officers: Dr. Benjamin Feuerstein, Bay Shore, President; Dr. Howard Wunderlich, Hicksville, Vice-President; Dr. John M. Knapp, Garden City, Treasurer; Dr. Jerome Zwanger, 126 Hicksville Road, Massapequa, Secretary.

NORTHEASTERN NEW YORK RADIOLOGICAL SOCIETY

Officers of the Northeastern New York Radiological Society elected for the coming year are: President, Richard Batt, M.D., Glens Falls; Viee-President, Kencil Mitton, M.D., Schenectady; Secretary-Treasurer, Irving Van Woert, Jr., M.D., Albany Hospital, Albany.

OHIO STATE RADIOLOGICAL SOCIETY

At a recent meeting of the Ohio State Radiological Society, the following officers were elected: President, Paul Jones, M.D., Zanesville; Vice-President and President-Elect, John R. Hannan, M.D., Cleveland; Secretary, Francis C. Curtzwiler, M.D., 421 Michigan St., Toledo 2; Treasurer, Frances A. Miller, M.D., Youngstown.

OREGON RADIOLOGICAL SOCIETY

The Oregon Radiological Society at a recent meeting elected the following officers for the ensuing year: Dr. J. Wayne Loomis, President; Dr. Norman L. Bline, President-Elect; Dr. C. V. Allen, 9855 S. W. Hawthorne Lane, Portland, Secretary-Treasurer.

CENTRE ANTOINE BÉCLERE

The new president of the Centre Antoine Béclère des Relations Internationales en Radiologie Médicale is Professor Antoine Lacassagne, who succeeds the late Professor A. Baudouin. Other nominations ratified at the time of Professor Lacassagne's election are: to the Administrative Council, Professor Madrazo of Mexico, Professor Schinz of Zurich, and Professor Dognon of Paris. Vice-presidents are Dr. A. Dariaux, Dr. H. Desgrez, and Professor P. Harvier.

SOCIETY OF NUCLEAR MEDICINE

Newly elected officers of the Society of Nuclear Medicine include the following: President, Marshall Brucer, M.D., Oak Ridge, Tenn.; President-Elect, Henry L. Jaffe, M.D., Los Angeles, Calif.; Vice-President, Franz Bauer, M.D., Los Angeles, Calif.: Vice-President Elect, Dwight E. Clark, M.D., Chicago, Ill.; Secretary, Robert W. Lackey, M.D., 452 Metropolitan Bldg., Denver 2, Colo.; Treasurer, Lindon Seed, M.D., Chicago, Ill.

At the Society's fourth annual meeting held in Oklahoma City in June 1957, 334 new members were elected to the society. Forty-one papers in the field of medical applications of radioactive isotopes were presented, and under the direction of Dr. Marshall Brucer a refresher course on tracer technics in thyroid diagnosis was given.

Next year's meeting will be held June 19, 20, and 21 in Los Angeles.

Books Received

Books received are acknowledged under this heading, and such notice may be regarded as recognition of the courtesy of the sender. Reviews will be published in the interest of our readers and as space permits.

THE SALIENT POINTS AND THE VALUE OF VENOUS ANGIOCARDIOGRAPHY IN THE DIAGNOSIS OF THE CYANOTIC TYPES OF CONGENITAL MALFORMATIONS OF THE HEART: A TEN YEAR STUDY OF 421 ANGIOCARDIOGRAMS DONE ON 283 PATIENTS. By BENJAMIN M. GASUL, M.D., GERSHON HAIT, M.D., ROBERT F. DILLON, M.D., and EGBERT H. FELL, M.D. A volume of 80 pages, with 42 figures and 4 tables. Published by Charles C Thomas, Springfield, Ill., 1957. Price $3.50.

SELECTED PAPERS FROM THE INSTITUTE OF CANCER RESEARCH, ROYAL CANCER HOSPITAL, AND FROM THE ROYAL MARSDEN HOSPITAL, 1954. Published by order of the Committee of Management of the Institute and the Board of Governors of the Royal Marsden Hospital, London. Volume 9. A volume of 904 pages with figures and tables. Printed by the Replika Process in Great Britain by Lund Humphries, London, England, 1957.

MALADIES DES VEINES: DIAGNOSTIC ET TRAITEMENT. By CLAUDE OLIVIER, Agrégé de la Faculté de Médecine de Paris, Chirurgien des Hôpitaux. Preface by Professor H. Mondor. A volume of 600 pages, with 342 figures and 1 colored plate. Published by Masson & Cie, Editeurs, 120, Boulevard Saint-Germain, Paris, 6e, France, 1957. Price 6,700 francs (paper bound); 7,400 francs (cloth).

RADIOLOGIE CLINIQUE DE L'ESTOMAC OPÉRÉ. By P. PORCHER, Médecin Radiologiste de l'Hôpital Saint-Antoine et de l'Hôpital Américain, Membre de l'Académie de Chirurgie, and P. BUFFARD, Médecin Radiologiste des Hôpitaux de Lyon, with the collaboration of R. GUILLET, Professeur agrégé de Chirurgie de la Faculté de Médecine de Lyon, and CL. COUINAUD, Assistant de Chirurgie des Hôpitaux de Paris. Preface by F. Moutier. A volume of 660 pages, with 507 figures. Published by Masson & Cie, Editeurs, 120, Boulevard Saint-Germain, Paris, 6e, 1957. Price 7,200 francs (paper bound); 8,000 francs (cloth).

SELEKTIVE LUNGENANGIOGRAPHIE IN DER PRÄOPERATIVEN DIAGNOSTIK UND IN DER INNEREN KLINIK. By PROF. DR. WILHELM BOLT, Medizinische Universitätsklinik Köln, PROF. DR. WERNER FORSSMANN, Bad Kreuznach, and DR. HANS RINK, Landesmed.-Direktor, Rheinisches Landeskrankenhaus Marienheide. With a Foreword by Prof. Dr. h. c. H. W. Knipping, Direktor der Medizinischen Universitätsklinik Köln. A volume of 200 pages, with 205 figures. Published by George Thieme Verlag, Stuttgart, Germany, 1957. Distributed in the United States and Canada by the Intercontinental Medical Book Corporation, New York 16, N. Y. Price, DM 54.—($12.85).

Book Reviews

POSITIONING IN RADIOGRAPHY. By K. C. CLARK, M.B.E., F.S.R., Honorary Fellow and Past President, Society of Radiographers; Radiographer, Princess Mary's Hospital (for Surgical Tuberculosis) and Margate (General) Hospital, 1922-27; Radiographer-in-Charge, Royal Northern Hospital, London, 1927-35; Tutor to X-ray Training School, 1930-35; Lecturer in Radiographic Technique for Postgraduate Courses in Medical Radiology, from 1940, D.M.R.E.; from 1942 D.M.R. (London), from 1951 D.M.R. (Diagnosis), University of London, British Postgraduate Medical Federation; responsible for lecture course, Joint Hospitals Radiographic School (Charing Cross, University College and Westminster) for the Membership Diploma of the Society of Radiographers (M.S.R.) from 1953: Principal of the Department of Radiography and Medical Photography of Ilford Limited from 1935. A volume of 656 pages, with 2,150 illustrations. Published by Grune & Stratton, Inc., New York Seventh edition, 1956. Price $29.00.

Clark's superb work on Positioning in Radiography made its first appearance in 1939, and subsequent editions appeared in rapid succession. In this seventh edition, there are added 600 new illustrations and 100 pages of technical information to make the text a classical compilation. New sections on Macroradiography and additional information on Radiation Exposure have been included.

For those who are committed to the training of student technicians, this work should prove of invaluable assistance; for those who seek aid in diagnostic procedures, it will be most helpful. It should be available for first-hand reference in every x-ray laboratory.

RETROPNEUMOPERITONEUM UND PNEUMOMEDIASTINUM. By Prof. Dr. UMBERTO COCCHI, ZÜRICH. With a Foreword by Prof. Dr. H. R. Schinz. Fortschritte auf dem Gebiete der Röntgenstrahlen und der Nuklearmedizin, Ergänzungsband 79. A volume of 226 pages, with 285 illustrations included on 142 figures. Published by Georg Thieme Verlag, Stuttgart, Germany, 1957. Distributed in the United States and Canada by Intercontinental Medical Book Corporation, New York 16, N. Y. Price DM 75.—($17.85); to subscribers, DM 67.50.

In this excellent monograph the author presents a comprehensive discussion of the introduction of gas into the retroperitoneal space and the mediastinum for diagnostic purposes, with a wealth of information regarding this relatively new procedure which otherwise could be obtained only by a time-consuming study of many articles in various specialty journals.

Pneumoretroperitoneum is said to be much less dangerous and more informative than pneumoperitoneum and to deserve more frequent use. In fact, if properly carried out, and if the contraindications are observed, the procedure is not more dangerous than ordinary intravenous pyelography. Of the various procedures, the author gives preference to the perineal method of injection. Oxygen is used rather than air because it is much more quickly absorbed. The technic is described, and indications and side reactions are outlined.

In the clinical section of the book, the various organs—kidneys, adrenals, pancreas, liver, spleen, etc.—are discussed separately and, for each, interesting clinical cases are presented. Sectional (tomographic) radiographs are considered essential. The radiographic reproductions are excellent, and many of the tomograms are elucidated by explanatory sketches.

The chapter on the adrenals is particularly extensive. The anatomy, physiology, and pathology are

clearly described. It is in this field that pneumoretroperitoneum is supreme, affording diagnostic information that cannot be obtained by any other means.

The pancreas can be clearly studied by pneumoretroperitoneum combined with gas inflation of the stomach. If lateral tomographic films are taken, a cross-section of every inch of the pancreas can be shown between two layers of air.

Pneumomediastinum has a much narrower field of indication and usefulness, but in connection with tomography it may give valuable information concerning aneurysms, dermoid cysts, tumors of the thymus, the thyroid, the lymph nodes, and the esophagus.

An extensive list of the world literature on both procedures is given. The text is easily read. Drawings and sketches make clear the technic. The book is systematic and should be of great value not only to the radiologist but also to the urologist, the general surgeon, and the internist.

LA POLYARTHRITE CHRONIQUE ÉVOLUTIVE. By L. ISEMEIN, Médecin des Hôpitaux de Marseille, and A.-M. FOURNIER, Médecin Électro-Radiologiste des Hôpitaux de Marseille, with the collaboration of P. CIAUDO, A. TRIFAUD, and CL. COURTIEUX. With a preface by Professor F. Coste, and a Foreword by Professor Ch. Mattéi. A monograph of 316 pages, with 192 figures, including roentgenograms. Published by Masson et Cie, 120, Boulevard Saint-Germain, Paris, 6e, 1956. Price 3,200 fr.

The fact that the senior authors of this interesting monograph are an internist and a radiologist underlines their avowed intention to correlate the clinical and the roentgen findings of "chronic evolutive polyarthritis". There are covered successively, as indicated by the chapter titles: definitions and general considerations (pp. 1–6), symptomatology, (pp. 7-22), clinical and laboratory tests (pp. 23–49), roentgen findings (pp. 51-157), clinical types (pp. 159-179), morbid anatomy (pp. 181-199), etiology (pp. 201-209), pathogenesis (pp. 211-220), diagnosis (pp. 221-232), prognosis (pp. 233-235), and treatment (pp. 236-289). A bibliography and index complete the volume.

One may not agree with some of the opinions expressed. It is stated that the "Anglo-American" concept of rheumatoid arthritis is more comprehensive than that of chronic evolutive polyarthritis, the former including infectious polyarthritis and subacute curable rheumatism. On the other hand, among the radiologic aspects of the evolutive form, as related to etiologic classification, even psoriasis and gout are mentioned. Many other details are equally controversial. The relationship with the collagen diseases, for example, is touched upon cursorily, while the discussion appears to favor the pathogenetic interpretation of the condition as a disturbance of the neurovegetative system. In view of this, roentgen therapy over the cervical sympathetic chain is suggested in the hope of a systemic effect.

The best part of the book is the description of the roentgenologic findings. It begins with technical advice and recommends fine focus (1.0 mm.^{2} or less; preferably 0.3 mm.^{2}), low kilovoltage, high milliamperage, short exposure time, Bucky technic, and fine grain film in cardboard holder. This combination will produce excellent contrast and best possible detail. Magnification procedures are said to be of only didactic value, while other methods, such as body-section roentgenography, or pneumoarthrography, appear to be of limited or incidental help. The lesions encountered are very well described, and emphasis is placed on the phase of the disease at which certain roentgenologic findings may be expected. The extensive clinical experience of the authors is demonstrated by the rich material presented in the form of excellent reproductions.

Notwithstanding the many shortcomings of this text, it ought to be consulted by all those who are particularly interested in rheumatoid arthritis, if only because it presents, in a highly palatable form, the French point of view on this subject.

RADIOLOGICAL SOCIETY OF NORTH AMERICA

FORTY-THIRD ANNUAL MEETING: PRELIMINARY PROGRAM

Palmer House, Chicago, Illinois, Nov. 17-22, 1957

Monday, November 18

OPENING SESSION: 2:00–4:30 P.M.

SECTION AB

Richard H. Chamberlain, M.D., First Vice-President Presiding

Call to Order.

Greetings and Introductions.

President's Address. C. EDGAR VIRDEN, M.D.

Memorial Fund Lecture. The Natural History of Multiple Myeloma Before Radiological Evidence of Disease. ELLIOTT F. OSSERMAN, M.D. Introduced by FREDERICK W. O'BRIEN, SR., M.D.

Symposium on Reactions from Intravenous Organic Iodide Compounds. EVERETT L. PIRKEY, M.D., *Moderator*. HENRY P. PENDERGRASS, M.D.,* EUGENE P. PENDERGRASS, M.D., RODERICK L. TONDREAU, M.D., PETER K. KNOEFEL, M.D.,* JOHN A. EVANS, M.D.,* NATHANIEL FINBY, M.D., ISRAEL STEINBERG, M.D., LAWRENCE A. DAVIS, M.D.,* JOHN F. WEIGEN, M.D.,* SYDNEY F. THOMAS, M.D.

BUSINESS MEETING: 4:30 P.M.

Tuesday, November 19

SECTION A: 10:30 A.M.–12:30 P.M.

Maurice D. Frazer, M.D., Second Vice-President Presiding

Regional Manifestations of Scleroderma. WILLIAM T. MESZAROS, M.D.

Relationship Between Cardiac Failure and Gastric Ulcer in the Older Age Group. MICHAEL M. KLEIN, M.D.

Infarction of the Small Intestine. RICHARD H. MARSHAK, M.D., BERNARD S. WOLF, M.D., and JOAN ELIASOPH, M.D.

Functional Disturbances of the Gastrointestinal Tract. THOMAS E. MACHELLA, M.D.

Emotions and Altered Roentgen Patterns in the Gastrointestinal Tract. ROY R. GREENING, M.D.

SECTION B: 10:30 A.M.—12:30 P.M.

PATIENT EXPOSURE IN DIAGNOSTIC PROCEDURES

Russell H. Morgan, M.D., Presiding

Radiation Dose in Diagnostic X-Ray Procedures. T. A. LINCOLN, M.D., and E. D. GUPTON, M.S.*

Gonadal Exposure Dose from Diagnostic X-Ray Procedures. ARNOLD FELDMAN, M.S.,* GEORGE C. BABCOCK, M.D., DIMITRY MORKOVIN, Ph.D., M.D., and RAYMOND R. LANIER, Ph.D., M.D.

Radiation Dose Incident to Diagnostic X-Ray Procedures. R. GARRETT, M.S., O. TAMUZS, M.S., M. L. MEURK, B.A., J. S. LAUGHLIN, Ph.D.,* and R. S. SHERMAN, M.D.

Some Useful Radiation Protection Technics. S. J. VACIRCA, M.S.

Radiation Safety Evaluation of Fluoroscopes. ROBERT OWEN GORSON, M.S.,* JOHN HALE, Ph.D., DAVID KUSNER, B.A., and JAMES R. BARTSCH, R.T.

SECTION AB: 2:00–4:30 P.M.

Laurence L. Robbins, M.D., Presiding

The Rad. H. M. PARKER, M.Sc., and RICHARD H. CHAMBERLAIN, M.D.

Orthovoltage Rotation Therapy: Six Years Experience in a General Hospital. MORTON M. KLIGERMAN, M.D.,* NORAH DU V. TAPLEY, M.D., and CHARLES DI LIBERTI, M.D.

Studies of Time-Dose Relationship: The Effect of Fractionation. WILLIAM R. EYLER, M.D.,* LUCILLE A. DU SAULT, M.S., and WENDELL M. BURNS, M.D.

Radioactive Gold in the Treatment of Carcinoma of the Prostate. H. B. ELKINS, M.D.,* R. H. FLOCKS, M.D., and D. A. CULP, M.D.

The Use of Radioactive Gold in the Treatment of Cancer of the Cervix. WILLARD M. ALLEN, M.D.

Circulation and Growth of Epithelioma and Adenocarcinoma. MAURICE LENZ, M.D.

BUSINESS MEETING: 4:30 P.M.

Wednesday, November 20

SECTION A: 10:30 A.M.–12:30 P.M.

Harold P. Tompkins, M.D., Third Vice-President Presiding

Hydrocarbon Pneumonitis: An Evaluation of the Roentgen Findings in Sixty Cases. FREDERICK J. BONTE, M.D.

Pulmonary Torulosis. LEWIS G. JACOBS, M.D.

Roentgen Patterns of Primary Lung Tumors Related to Survival. GWILYM S. LODWICK, M.D., THEODORE E. KEATS, M.D.,* and JOHN DORST, M.D.

Variability of the Radiographic Pattern of Non-Fatal Pulmonary Histoplasmosis. JOSEPH W. PEABODY, JR., M.D.,* SOL KATZ, M.D., and EDGAR W. DAVIS, M.D.

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* Will present paper.

Bronchiolar Carcinoma. J. H. WOODRUFF, JR., M.D.
Current Management of Pulmonary Tuberculosis. ANTON M. PATONE, M.D., KARL H. PFUETZE, M.D., HIRAM T. LANGSTON, M.D., and MYRON MELAMED, M.D.

SECTION B: 10:30 A.M.–12:30 P.M.

COBALT-60 THERAPY

Robert Robbins, M.D., Presiding

Outline of Probable World Requirements of Cobalt-60 for Therapy Machines. R. F. ERRINGTON., M. A.
A Comparison of a Cobalt-60 Teletherapy Machine and a 2-MEV Van de Graaff X-Ray Generator on Basis of Physical Measurements. K. C. TSIEN, M.A.,* and ROBERT ROBBINS, M.D.
Transit Dose Measurements in Rotation Therapy. PAUL M. PFALZNER, M.Sc.
The Use of Idealized Body Contours in Cobalt-60 Rotation Dosimetry. ROBERT H. HAYNES, B.Sc., and GERD FROESE, M.Sc.*
Cobalt-60 Radiation Measurement. C. B. BRAESTRUP, B.S., and R. MOONEY, M.Sc.*

SECTION AB: 2:00–5:00 P.M.

Theodore J. Wachowski, M.D., Presiding

Effect of Splenic Irradiation, Radioisotopes, Chemotherapeutic Agents, and Steroids upon the Histopathology of the Spleen of Patients with Leukemia and Lymphomas. MATTHEW BLOCK, Ph.D., M.D.
Influence of Drugs on Radiation Reactions of Tumors in Mice. HENRY P. PLENK, M.D.
Clinical Significance of Radiation Changes in Normal Vaginal Mucosa. RAYMOND R. LANIER, M.D.,* and WALTER T. WIKLE, M.D.
Contrast Visualization of the Lymph Nodes. NORMAN ZHEUTLIN, M.D.,* and EDWARD SHANBROM, M.D.
Problems in Reduction of Radiation Dosage in Diagnostic Procedure. EARL R. MILLER, M.D., *Moderator.* HYMER L. FRIEDELL, M.D., RUSSELL H. MORGAN, M.D., LAURISTON S. TAYLOR, A.B., and JOHN E. JACOBS.

SECTION C: 2:00–5:00 P.M.

RECENT ADVANCES IN RADIOLOGIC PHYSICS

H. O. Wyckoff, Ph.D., Presiding

This program is arranged only a few weeks before the meeting, and details are therefore not available.

Thursday, November 21

SECTION A: 10:30 A.M.–12:30 P.M.

Robert Burns Lewis, M.D., Presiding

Occlusive Cerebrovascular Disease. JAMES E. LOFSTROM, M.D., *Moderator.* JACOB L. CHASON, M.D., JOHN STERLING MEYER, M.D., MAURICE TATELMAN, M.D., and J. E. WEBSTER, M.D.
Visualization of the Coronary Vessels in Man: A Practical Method. CHARLES T. DOTTER, M.D.,* and LEWIS H. FRISCHE, M.D.
Selective Angiocardiography of Atrial Septal Defects. ULF G. RUDHE, M.D.
Emphysema by Microradiography. CHARLES P. ODERR, M.D.,* PHILIP PIZZOLATO, M.D., and JOSEPH ZISKINO, M.D.
Obstructive Pulmonary Emphysema: Physiological Abnormalities. HURST B. HATCH, Jr., M.D.

SECTION B: 10:30 A.M.–12:30 P.M.

NEUTRON REACTORS AND RADIOBIOLOGY

George LeRoy, M.D., Presiding

SYMPOSIUM: NUCLEAR REACTOR INSTALLED AT NATIONAL NAVAL MEDICAL CENTER, BETHESDA

Capt. S. F. Williams, MC, USN, Moderator

(*a*) Physical Factors of a Low Power Medical Reactor. CDR. T. E. SHEA, MSC, USN,* and LIEUT. ROBERT SHARP, MSC, USN.
(*b*) Medical Applications of Neutron Activation Analysis. LIEUT. T. G. MITCHELL, MSC, USN,* and LIEUT. R. P. SPENCER, MC, USNR.
(*c*) Production and Use of Short Half-Life Radioisotopes in Clinical Medicine. CAPT. D. R. KING, MC, USN,* and LIEUT. W. S. MAXFIELD, MC, USNR.
(*d*) THE AGN-201 Reactor—THE THERMAL COLUMN. CDR. F. W. CHAMBERS, MSC, USN,* and LIEUT. JAMES W. DUCKWORTH, MSC, USN.

Ability of the Fetal Retina to Reconstitute After an Insulting Dose of X-Radiation. ROBERTS RUGH, Ph.D.,* and JOAN WOLFF.
Strandqvist Plot of Radiation Cataracts. ELIZABETH F. FOCHT, B.A., and GEORGE R. MERRIAM, Jr., M.D.
Differences in the Effect of Breathing Oxygen on the Radiosensitivity of Normal and Malignant Tissues. PAUL HOWARD-FLANDERS, Ph.D.

SECTION AB: 2:00–4:30 P.M.

Charles M. Gray, M.D., Presiding

Osteomyelitis of the Mandible Following Irradiation. ROBERT S. STONE, M.D., *Chairman;* ELMER NG, M.D., FRANK CHAMBERS, M.D., HARRY S. OGDEN, M.D., and GRANVILLE C. COGGS, M.D.
Co^{60}-Beam Therapy in Carcinoma of the Esophagus. J. S. LOTT, M.D.,* and IVAN H. SMITH, M.D.
Pediatric Symposium. JOHN W. HOPE, M.D., *Moderator.* JOHN BIGLER, M.D., JOHN H. HARRIS, M.D., JOHN KIRKPATRICK, M.D., C. E. KOOP, M.D., HARVEY WHITE, M.D., M. H. WITTENBORG, M.D.

BUSINESS MEETING: 4:30 P.M.

THE CARMAN LECTURE: 8:30 P.M.

The Treatment of Carcinoma of the Breast
L. Henry Garland, M.D.

Friday, November 22

SECTION A: 10:30 A.M.–1:00 P.M.

H. Milton Berg, M.D., Presiding

Axial Transverse Body-Section Radiography of the Chest. STEFAN P. WILK, M.D.

Pancreatic Pneumotomography. HANS LUDIN, M.D.,* THANE ASCH, M.D., and JOHN A. EVANS, M.D.

The Lumbosacral Spine. John R. WINSTON, M.D., *Moderator*. RALPH K. GHORMLEY, M.D., WAYNE A. SIMRIL, M.D., ROBERT D. MORETON, M.D., and JAMES K. STACK, M.D.

SECTION B: 10:30 A.M.–1:00 P.M.

DOSIMETRY

Harald H. Rossi, Ph.D., Presiding

Local Absorbed Dose Determination by Direct Calorimetric Means. S. GENNA, M.S., P. MILVY, B.S.,* and J. S. LAUGHLIN, Ph.D.

Comparison of Theoretical and Experimental Filtered X-Ray Spectra. HARRY H. HUBBELL, Ph.D.,* JOSEPH S. CHEKA, B.A., and F. H. WALDEMAR NOLL, Ph.D.

Dose Distribution About Large Circular and Linear Sources of Gamma Radiation. I. F. HUMMON, M.D., and R. S. LANDAUER, Ph.D.*

A Body-Cavity Radiation Dosimeter. FRANK E. HOECKER, Ph.D., and HOMER L. HIEBERT, M.D.

A Limited Survey of Radiation Exposure from Dental X-Ray Units. ROBERT OWEN GORSON, M.S.,* RONALD M. HALVORSEN, B.S., JESSE LIEBERMAN, M.S., and EDWARD V. AITKEN, B.S.

REFRESHER COURSES: POSTGRADUATE INSTRUCTION

The 1957 Refresher Course Series will be presented during the Forty-third Annual Meeting of the Radiological Society of North America at the Palmer House, Chicago, Ill. Registration for the meeting will begin at 1:00 P.M., Saturday, Nov. 16. On Sunday, Nov. 17, the registration desk will be open at 9:00 A.M.; Monday through Friday it will be open at 8:00 A.M. Please register early. The Courses will begin at 2:00 P.M., Sunday, Nov. 17, with the Therapy Information Session. This will be followed by a series of five Courses, running from 4:30 to 6:30 P.M. The Film Reading Session will begin at 7:30 P.M.

On Monday, Nov. 18, there will be a series of Refresher Courses beginning at 8:30 A.M. and continuing until 10:00 A.M., with a second series from 10:30 A.M. until noon. The remainder of the week the Refresher Course period will be from 8:30 to 10:00 A.M. No other meeting will be scheduled during the hours in which the Refresher Courses are conducted. Attendance is limited to the medical profession, including graduate students and residents in radiology; radiation physicists, radiobiologists, chemists and others closely concerned with the science of radiology; and medical students certified by the deans of their respective medical schools.

A registration fee of $15.00, which includes the Refresher Course fee, must be paid by all non-members of the Radiological Society of North America at the time of registration at the Palmer House. The exceptions are guest speakers, guest instructors, scientific exhibitors, residents or fellows in radiology, medical students, trainees in physics, and officers in the Armed Forces of the United States on temporary duty and away from their practice. Members of the Radiological Society of North America do not pay a registration fee or a Refresher Course fee. All, however, must register at the R.S.N.A. registration desk in the Palmer House. Admission to the Refresher Courses will be by presentation of the registration badge and a ticket for the particular Course, except Courses No. 1, which is the Therapy Information Session on Sunday afternoon, and No. 7, the Film Interpretation Session held on Sunday evening. Admission to these Courses will be by badge only. Payment of the registration fee by non-members is *not* to accompany the request for tickets but is to be paid when the tickets are called for at the registration desk. If you cannot use the tickets you have reserved, please notify the Chairman of the Refresher Course Committee.

One important change in the Refresher Course Program is to be noted: Namely, the addition of a new series of Courses on Sunday afternoon and a second series of Courses on Monday morning. This is an attempt to answer the question asked on innumerable occasions: "Why can't we have more time to attend Refresher Courses?"

Read the description of the Courses, noting particularly the days that they are offered, and make your selection for the day. Turn to the colored insert, indicate thereon your first, second, and third preferences, and mail the order blank promptly. The number attending each course will be limited by the seating capacity of the room. The requests for tickets will be filled in chronological order. You will be notified regarding your selection.

After you have gone over these courses, we would appreciate suggestions for future courses, as well as for new instructors for some of the present ones. Please put these suggestions on a card and leave it at the registration desk at the time you pick up your tickets, or mail it to the Chairman at the time you make your request.

Course No. 1: Sunday, 2:00–4:00 P.M.

Therapy Information Session

SYDNEY F. THOMAS, M.D., Palo Alto, Calif.
Moderator

HOWARD E. SKIPPER, Ph.D., Birmingham, Ala.
JAMES F. HOLLAND, M.D., Buffalo, N. Y.
LAURENS P. WHITE, M.D., San Francisco, Calif.
JOHN W. FROST, M.D., Philadelphia, Penna.
ANTOLIN RAVENTOS, M.D., Philadelphia, Penna.
THOMAS C. POMEROY, M.D., Columbus, Ohio

This course is designed to bring before radiologists the chemotherapeutic approach to cancer, as it has been and is being used today. The fundamental chemical actions of some drugs will be reviewed, including a consideration of the similarities to radiation effects. The lymphoma-leukemia group will be emphasized, teamwork type of management being the keynote. The approach to solid tumors will be discussed. Individual case presentations and discussion by the panel with questions from the floor will be in order.

Course No. 2: Sunday, 4:30–6:00 P.M.

Treatment of Pelvic Cancer

MANUEL GARCIA, M.D.
New Orleans, La.
and
WALTER T. MURPHY, M.D.
Buffalo, N. Y.

A greater portion of the first period will be devoted to radiation treatment of cancers of the cervix uteri. The second period will cover treatment of cancer of the corpus and its appendages.

(This course continued Monday, Course No. 11)

Course No. 3: Sunday, 4:30–6:00 P.M.

The Physiodynamics of the Lesser Circulation with Practical Application as Found in Daily Practice and as of Interest to the Radiologist, the Clinician, and the Surgeon

W. W. WASSON, M.D.
Denver, Colo.

I. A brief historical sketch of the researches which have made this presentation possible.
II. Anatomy and physiology of the lungs and the physiodynamics of the lesser circulation.
III. Discussion of cases illustrating the influences of physiodynamics of the lesser circulation:
1. Cor pulmonale in emphysema and lung fibrosis
2. Sudden death from lung embolus
3. The diaphragmatic syndrome and obesity
4. The closure of the ductus arteriosus
5. Hypoventilation and atelectasis
6. Mitral disease and lung congestion
7. Kyphosis and heart failure

Course No. 4: Sunday, 4:30–6:00 P.M.

Roentgen Evaluation of Bone Tumors: Relationship of Bone Destruction and Proliferation to Tumor Behavior

GWILYM S. LODWICK, M.D.
Columbia, Mo.

The purpose of this course is to provide a roentgenologic basis for predicting tumor behavior and a rational treatment of bone neoplasms. Survival statistics based upon a detailed analysis of roentgenograms from 1,221 cases will be presented. Those attending are invited to bring films.

Course No. 5: Sunday, 4:30–6:00 P.M.

Basic Electronics for Radiologists

CHARLES T. DOTTER, M.D., LOUIS H. FRISCHE, M.D.
Portland, Ore.

Electronic complexities have made appraisal of modern equipment increasingly difficult for the practicing radiologist, beleaguered as he is by other professional responsibilities. The objective of this course, therefore, is to review elementary principles, emphasizing everyday radiological applications. Operation of power supply, simple vacuum tubes, electronic switches, and similar devices will be discussed, supplemented by practical demonstration.

(*This course continued Monday, Course No. 12*)

Course No. 6: Sunday, 4:30–6:00 P.M.

Radiology of the Larynx and Pharynx

ARNOLD L. BACHMAN, M.D.
New York, N. Y.

The course will cover the radiographic anatomy and physiology of the larynx, radiology of laryngeal paralysis, radiology of normal and abnormal swallowing patterns, tumors of the larynx and pharynx, demonstration of extension of laryngopharyngeal tumors. In addition, certain benign conditions will be discussed, including foreign bodies in the cervical esophagus, cricopharyngeal spasm, and radiology of the adenoids.

(*This course continued Monday, Course No. 14*)

Course No. 7: Sunday, 7:30–9:30 P.M.

Film Interpretation Session

JOHN A. EVANS, M.D., New York, N. Y.
Moderator
WILLIAM R. EYLER, M.D., Detroit, Mich.
TED F. LEIGH, M.D., Emory University, Ga.
C. RICHARD PERRYMAN, M.D., Pittsburgh, Penna.
STANLEY M. WYMAN, M.D., Boston, Mass.

This session is a diagnostic symposium based upon proved cases which will be demonstrated at the time of the course. Every effort will be made to select cases that are of educational value and that will permit an orderly, analytical approach to a diagnostic problem. Key films will be displayed at the afternoon session so that the audience will have a chance to see some of the original material.

Any member of the Radiological Society who desires to present an instructive case may submit his material to the moderator, John A. Evans, M.D., 525 East 68th St., New York 21, N. Y.

Course No. 8: Monday, 8:30–10:00 A.M.

Important Considerations in the X-Ray Demonstration and Diagnosis of Fractures with Some Unusual Examples

KENNETH D. A. ALLEN, M.D., JOHN H. FREED, M.D.
Denver, Colo.

A brief discussion of technic and the various routine and special radiographic projections required to achieve a high accuracy in the radiographic demonstration and diagnosis of fractures will be presented, with numerous case illustrations. Examples illustrating problems in differential diagnosis, importance of follow-up examinations, management of complications, and interesting and unusual fractures will be shown. Comments will be made on methods of reporting fractures, advising and consulting with the referring physician, and avoiding medicolegal complications.

Course No. 9: Monday, 8:30–10:00 A.M.

Treatment Planning: Conventional Energy X-rays

A. RAVENTOS, M.D., and J. HALE, Ph.D.
Philadelphia, Penna.

Conventional-voltage x-rays can be used with great effectiveness in the treatment of superficial

lesions and also of many deep-seated lesions. To utilize fully the potentialities of conventional-voltage x-rays, it is necessary to have a good understanding of the physical principles involved and to practice careful treatment planning. This course will deal with the basic principles and some of the treatment planning methods that have proved useful. Some clinical problems requiring the use of very low, intermediate, and 250-kv x-ray beams will be discussed in detail.

Course No. 10: Monday, 8:30–10:00 A.M.

Mediastinal Masses

TED F. LEIGH, M.D., and H. STEPHEN WEENS, M.D.
Atlanta, Ga.

1. Anatomy and physiology of the mediastinum.
2. Tumors—of the thymus, thyroid, parathyroids, esophagus, peripheral nervous system, fat, lymph nodes, bone and cartilage, and others; teratomas, germinal tumors, mesotheliomas, mesenchymomas; tumors of blood vascular origin, and tumors of lymph vascular origin.
3. Cysts—bronchogenic, of digestive tract, pericardial, celomic and inflammatory, thymic, parasitic, and others.
4. Aneurysms—of the aorta, pulmonary artery, other arteries, and the veins.
5. Miscellaneous lesions—abscesses, diaphragmatic herniations, meningoceles, paramediastinal pulmonary lesions, and others.

(*This course continued at 10:30, Course No. 22*)

Course No. 11: Monday, 8:30–10:00 A.M.

Treatment of Pelvic Cancer

MANUEL GARCIA, M.D.
New Orleans, La.
and
WALTER T. MURPHY, M.D.
Buffalo, N. Y.

(*Continued from Sunday, Course No. 2*)

Course No. 12: Monday, 8:30–10:00 A.M.

Basic Electronics for Radiologists

CHARLES T. DOTTER, M.D., and L. H. FRISCHE, M.D.
Portland, Ore.

(*Continued from Sunday, Course No. 5*)

Course No. 13: Monday, 8:30–10:00 A.M.

Workshop
Therapeutic Uses of Radioisotopes

ROBERT ROBBINS, M.D., Philadelphia, Penna.
Moderator
R. KENNETH LOEFFLER, M.D., Madison, Wisc.
ANTOLIN RAVENTOS, M.D., Philadelphia, Penna.
H. B. ELKINS, M.D., Iowa City, Iowa
EUGENE L. SANGER, M.D., Cincinnati, Ohio
JOHN P. STORAASLI, M.D., Cleveland, Ohio

This will be an informal course with a discussion of specific clinical problems by various experienced users of radioactive isotopes. It is hoped that audience participation will be active and that the level of questions and discussion will be informative to those who are already users of isotopes.

Course No. 14: Monday, 8:30–10:00 A.M.

Radiology of the Larynx and Pharynx

ARNOLD L. BACHMAN, M.D.
New York, N. Y.

(*Continued from Monday, Course No. 6*)

Course No. 15: Monday, 8:30–10:00 A.M.

Basic Radiation Dosimetry

HAROLD O. WYCKOFF, Ph.D.
Washington, D. C.

The text for this course is the 1956 Recommendations of the International Commission of Radiological Units and Measurements.[1] The difference between the exposure dose in roentgens, the absorbed dose in rads, and the RBE dose in rems will be pointed out. Data on energy dependence and rate dependence of r-meters will be presented, and suggestions will be made on methods for checking the reproducibility of such instruments. Direct measurement of the absorbed dose by calorimetric means will be discussed, but the principal method considered will be computation of absorbed dose from ionization measurements.

[1] National Bureau of Standards Handbook 62.

Course No. 16: Monday, 10:30–12:00 A.M.

Professional Liability Problems

C. JOSEPH STETLER, Attorney
Chicago, Ill.

During the past few years the American Medical Association has conducted an extensive survey and study of all phases of malpractice and medicolegal suits. A large volume of data and material has been gathered. Some phases of these suits will be reviewed to show how they were initiated and how they could have been circumvented.

Course No. 17: Monday, 10:30–12:00 A.M.

Translumbar Aorto-Arteriography

GEORGE D. DAVIS, M.D.
Rochester, Minn.

The aims, technical problems, and various methods of aortography and femoral arteriography *via* the aorta will be reviewed. More emphasis will be placed on the study of vascular occlusive disease

PLAN OF PRESENTATION

SUNDAY, Nov. 17
2:00–4:00 P.M.

1. Therapy Information Session
Sydney F. Thomas, M.D.
Moderator
Howard E. Skipper, Ph.D.
James F. Holland, M.D.
Laurens P. White, M.D.
John W. Frost, M.D.
Antolin Raventos, M.D.
Thomas C. Pomeroy, M.D.

4:30–6:00 P.M.

2. Treatment of Pelvic Cancer (to be continued Monday)
Manuel Garcia, M.D.
Walter T. Murphy, M.D.

3. Physiodynamics of Lesser Circulation
W. W. Wasson, M.D.

4. Roentgen Evaluation of Bone Tumors
Gwilym S. Lodwick, M.D.

5. Basic Electronics for Radiologists (to be continued Monday)
Charles T. Dotter, M.D.
Louis H. Frische, M.D.

6. Radiology of the Larynx and Pharynx (to be continued Monday)
Arnold L. Bachman, M.D.

7:30–9:30 P.M.

7. Film Interpretation Session
John A. Evans, M.D.
Moderator
William R. Eyler, M.D.
Ted F. Leigh, M.D.
C. Richard Perryman, M.D.
Stanley M. Wyman, M.D.

MONDAY, Nov. 18
8:30–10:00 A.M.

8. Important Considerations in X-ray Diagnosis of Fractures
Kenneth D. A. Allen, M.D.
John H. Freed, M. D.

9. Treatment Planning: Conventional Energy X-rays
A. Raventos, M.D.
J. Hale, Ph.D.

10. Mediastinal Masses (To be continued at 10:30)
Ted F. Leigh, M.D.
H. Stephen Weens, M.D.

11. Treatment of Pelvic Cancer (Continued)
Manuel Garcia, M.D.
Walter T. Murphy, M.D.

12. Basic Electronics for Radiologists (Continued)
Charles T. Dotter, M.D.
Louis H. Frische, M.D.

13. Workshop: Therapeutic Uses of Radioisotopes
Robert Robbins, M.D., Moderator, et al.

14. Radiology of the Larynx and Pharynx (Continued)
Arnold L. Bachman, M.D.

15. Basic Radiation Dosimetry
H. O. Wyckoff, Ph.D.

MONDAY, Nov. 18
10:30 A.M.–12:00

16. Professional Liability Problems
C. Joseph Stetler (Attorney)

17. Translumbar Aorto-arteriography
George D. Davis, M.D.

18. Diseases of Joints and Periarticular Tissues
Lester W. Paul, M.D.

19. Design and Equipment of Radioisotope Laboratories
G. W. Morgan

20. Wanted: A 250-KV X-ray Machine
Milton Friedman, M.D.

21. Examination of the Gastrointestinal Tract in Infants and Children (To be continued Tuesday)
Lawrence A. Davis, M.D.

22. Mediastinal Masses (Continued)
Ted F. Leigh, M.D.
H. Stephen Weens, M.D.

23. Neuroradiology (To be continued Tuesday)
Alfred L. Schmitz, M.D.

TUESDAY, Nov. 19
8:30–10:00 A.M.

24. Treatment Planning with High Energy Radiation (Particularly Telecobalt)
Lucille A. Du Sault, M.A.
Robert J. Bloor, M.D.

25. The Physiopathology of Practice
L. Henry Garland, M.D.

26. Therapeutic Uses of Radioisotopes
W. K. Sinclair, Ph.D.

27. The Small Intestine (To be continued Wednesday)
Richard H. Marshak, M.D.

28. Roentgen Cardiology (To be continued Wednesday)
Melvin M. Figley, M.D.

29. Examination of the Gastrointestinal Tract in Infants and Children (Continued)
Lawrence A. Davis, M.D.

30. Common Causes of Radiation Hazards
Carl B. Braestrup, B.S., P.E.
Theodore P. Eberhard, M.D.

31. Neuroradiology (Continued)
Alfred L. Schmitz, M.D.

WEDNESDAY, Nov. 20 8:30–10:00 A.M.	THURSDAY, Nov. 21 8:30–10:00 A.M.	FRIDAY, Nov. 22 8:30–10:00 A.M.
32. **Bone Tumors (To be continued Thursday)** Robert D. Moseley, M.D.	40. **Bone Tumors (Continued)** Robert D. Moseley, M.D.	47. **Aspects of Roentgen Therapy in Childhood** M. H. Wittenborg, M.D.
33. **Radiation Exposure and Protection with Various Diagnostic Procedures** M. L. Meurk, B.A. R. S. Sherman, M.D.	41. **Dosage in Internal Use of Radium and other Radioisotopes as Discrete Sources** Elizabeth F. Focht, B.A.	48. **Useful Aids, Gadgets and Appliances for X-ray and Radium Therapy** Jesshill Love, M.D.
34. **Treatment Planning in Rotation Therapy** Morton M. Kligerman, M.D. Edith H. Quimby, Sc.D.	42. **Fundamentals in Chest Roentgen Interpretation (To be continued Friday)** Benjamin Felson, M.D.	49. **Fundamentals in Chest Roentgen Interpretation (Continued)** Benjamin Felson, M.D.
35. **The Small Intestine (Continued)** Richard H. Marshak, M.D.	43. **Genetic Effects of Radiation** W. L. Russell, Ph.D.	50. **Fundamental Considerations in Radiation Biology** Titus C. Evans, Ph.D.
36. **Roentgen Cardiology (Continued)** Melvin M. Figley, M.D.	44. **Roentgen Examination of the Sinuses and Mastoids (To be continued Friday)** Barton R. Young, M.D.	51. **Roentgen Examination of the Sinuses and Mastoids (Continued)** Barton R. Young, M.D.
37. **Diagnostic Applications of Radioactive Isotopes** H. L. Friedell, M.D. J. S. Krohmer, M.A.	45. **The Statistical Point of View (To be continued Friday)** Harold Tivey, M.D.	52. **The Statistical Point of View (Continued)** Harold Tivey, M.D.
38. **Irradiation Therapies for Carcinoma of the Urinary Bladder** J. R. Maxfield, Jr., M.D.	46. **Radiotherapy in Ophthalmology** George R. Merriam, Jr., M.D.	53. **Radium Therapy** John D. Reeves, M.D.
39. **Dental Roentgenography** Stanley A. Lovestedt, D.D.S.		

than on renal artery study. The technic and results of the method currently employed at the instructor's institution will be reviewed in detail. Stress will be placed on the importance of visualizing the femoral arteries during aortography, and a method of accomplishing this will be presented. Correlation between the roentgenologic appearances, functional impairment, and surgical considerations will be discussed.

Course No. 18: Monday, 10:30–12:00 A.M.

Diseases of Joints and Peri-articular Tissues

LESTER W. PAUL, M.D.
Madison, Wisc.

Following a brief discussion and illustration of the anatomy of a joint, with particular reference to the structures important in the production of roentgen abnormalities, the course will cover the common and some of the unusual lesions of the joints and peri-articular tissues. Correlation of the roentgen and pathologic findings will be made wherever possible. Emphasis will be placed upon the early changes caused by disease and upon differential diagnosis. A working classification of diseases of the joints will be given. Among the conditions which will be presented in some detail are rheumatoid arthritis and degenerative disease of the peripheral joints, and tumors and tumor-like processes of the intra-articular and peri-articular tissues.

Course No. 19: Monday, 10:30–12:00 A.M.

Design and Equipment of Radioisotope Laboratories

G. W. MORGAN
Oak Ridge, Tenn.

Practical aspects of the design and equipment of medical radioisotope laboratories will be discussed, with suggested facilities for different programs utilizing various radioisotopes. Prototype laboratories and facilities will be presented for both diagnostic and therapeutic programs. A review will be made of laboratories for use of radioisotopes purchased in a form standardized and ready for use as well as for hospitals procuring their isotopes directly from Atomic Energy Commission facilities. The discussion will also include facilities and equipment for private practitioners and typical hospital programs, as well as the more extensive programs involving animal experimentation.

Course No. 20: Monday, 10:30–12:00 A.M.

Wanted: A 250-kv X-Ray Machine: A Critical Evaluation of Supervoltage Therapy

MILTON FRIEDMAN, M.D.
New York, N. Y.

Although supervoltage irradiation has been employed clinically for more than twenty years, there is only a small amount of valid evidence in the literature that it produces increased survival rates. This is probably due to the fact that the radiation modality employed in the treatment of a cancer has a relatively small effect on the cure rate, while the biological nature of the tumor, its anatomical extent, and the skill of the therapist play major roles.

In an attempt to disclose the speaker's current value judgments, the following propositions will be discussed and illustrated.

1. Supervoltage irradiation has specific indications for certain stages or types of cancer of some organs.
2. It is becoming clear that supervoltage irradiation probably will not fulfill optimistic expectations in the treatment of certain cancers, such as those of the lung and esophagus.
3. 250-kv x-rays and radium employed with precision technics, and according to the concepts of radical irradiation therapy, can successfully compete with supervoltage in many cancers.
4. Certain lesions for which supervoltage irradiation originally had offered high hopes are probably better treated with 250-kv x-rays or radium.

Course No. 21: Monday, 10:30–12:00 A.M.

The Examination of the Gastrointestinal Tract in Infants and Children

LAWRENCE A. DAVIS, M.D.
Louisville, Ky.

Examination of the gastrointestinal tract in infants and younger children is difficult only in the technical problems involved. Actually, the range of abnormality is limited and does not compare with the complexity of disease found in the adult. The course will stress these technical problems, and offer suggestions for their solution by the radiologist and one technician. The various congenital and acquired diseases found in pediatric practice will be analyzed, and the use of water-soluble opaque media discussed.

(This course continued Tuesday, Course No. 29)

Course No. 22: Monday, 10:30–12:00 A.M.

Mediastinal Masses

TED F. LEIGH, M.D., and H. STEPHEN WEENS, M.D.
Atlanta, Ga.

(Continued from 8:30, Course No. 10)

Course No. 23: Monday, 10:30–12:00 A.M.

Neuroradiology

ALFRED L. SCHMITZ, M.D.
San Francisco, Calif.

Bone changes in meningiomas, acoustic nerve

tumors, and sellar tumors will be discussed. The technic and the normal roentgen anatomy in fractional encephalography will be illustrated. Normal encephalograms will be compared with those showing changes in the ventricular system and cisterns secondary to tumor pathology. Cerebral arteriograms will be presented to augment the encephalographic studies.

(*This course continued Tuesday, Course No. 31*)

Course No. 24: Tuesday, 8:30–10:00 A.M.

Treatment Planning with High Energy Radiation (Particularly Telecobalt)

LUCILLE A. DU SAULT, M.A., and ROBERT J. BLOOR, M.D.
Detroit, Mich.

Conventional isodose curves for a fixed source-skin distance will be compared with those developed primarily for use in rotation therapy with a fixed source-axis distance. Their use, the accuracy of the method, and corrections for absorption in actual tissues to be made in values calculated for unit-density material will be discussed. The dangers of "hot" spots, use of compensating filters and bolus, and differential "loading" of treatment fields will be illustrated.

Course No. 25: Tuesday, 8:30–10:00 A.M.

The Physiopathology of Practice Introduction to a Course on the Science and Art of Radiology

L. HENRY GARLAND, M.D.
San Francisco, Calif.

This course will attempt to outline certain aspects of various types of radiologic practice, hospital and office, governmental and private. Various forms of hospital-physician relationship will be analyzed, especially those under which the best type of radiologic service can be rendered to the patients.

In order to conserve time and permit discussion of newer trends, all participants will be assumed to have read and digested the official manual (*A Guide for Conduct of Radiologists in Relationships with Institutions*, American College of Radiology, 20 North Wacker Drive, Chicago, 1955). Questions already answered by that *Guide* will be regarded as tautologic. Specific questions submitted by registrants, in writing, will be answered.

Course No. 26: Tuesday, 8:30–10:00 A.M.

Therapeutic Uses of Radioisotopes

W. K. SINCLAIR, Ph.D.
Houston, Texas

Successful therapeutic use of radioisotopes depends on the deposition of a suitable amount of energy at the diseased site, with the minimum dissipation of energy elsewhere. This involves concentration of the radioactive material at the site in question, which may be achieved in a number of ways:

I. By metabolic accumulation of the isotope.
II. By the physical nature of the material (colloid).
III. By deliberate localization of specific sources.

I is limited to the use of radioiodine for thyroid disorders and, to a lesser extent, some other isotopes, such as phosphorus 32.

II includes the use of radioactive colloids, particularly gold 198 and chromic phosphate.

Under III, there are three main divisions: *intracavitary*, particularly in the bladder with solutions or point sources of cobalt 60, bromine 82, and gold 198; *interstitial*, which includes the use of needles, wires, and seeds of gold 198, tantalum 182, iridium 192, cesium 137, cobalt 60, and others; *superficial*, which includes some gamma-ray emitters such as tantalum-182 wire in the eye, but is concerned mainly with the application of beta emitters, phosphorus 32, and the plaques and shells of strontium 90 for the treatment of superficial lesions.

Each of these various applications will be reviewed with special reference to the dosimetry involved and with emphasis on group III.

Course No. 27: Tuesday, 8:30–10:00 A.M.

The Small Intestine

RICHARD H. MARSHAK, M.D.
New York, N. Y.

Part I

1. Technic, including a discussion of the various barium preparations.
2. Concepts of small intestinal patterns.
3. The malabsorption syndrome. Sprue, lymphosarcoma and Whipple's disease.
4. Problems in the interpretation of functional changes.
5. Barium studies in small intestinal obstruction.

Part II

1. Regional enteritis.
2. Infarction of the small bowel.
3. Tumors.
4. Miscellaneous disorders including scleroderma, amyloidosis, allergy.

(*The course continued Wednesday, Course No. 35*)

Course No. 28: Tuesday, 8:30–10:00 A.M.

Roentgen Cardiology

MELVIN M. FIGLEY, M.D.
Ann Arbor, Mich.

The first period will deal with the evaluation of the heart by simple examination in the assessment of alteration of cardiac physiology by diseases that are now amenable to surgical treatment.

The second period will be spent on the survey of methods by contrast opacification of the heart and their principal application.

(*This course continued Wednesday, Course No. 36*)

Course No. 29: Tuesday, 8:30–10:00 A.M.

The Examination of the Gastrointestinal Tract in Infants and Children

LAWRENCE A. DAVIS, M.D.
Louisville, Ky.

(*Continued from Monday, Course No. 21*)

Course No. 30: Tuesday, 8:30–10:00 A.M.

Common Causes of Radiation Hazards

CARL B. BRAESTRUP, B.S., P.E.
New York, N. Y.
and
THEODORE P. EBERHARD, M.D.
Ann Arbor, Mich.

The greatly increased potential exposure of the general population to ionizing radiation from many different sources has made it even more essential than previously to minimize the amount of exposure from the medical use of these agents.

The hazards associated with the medical use of roentgen rays may be minimized by the use of properly constructed equipment, ample room shielding and, most important, appropriate operating procedures. These factors will be discussed from the point of view of the safety of the patient, staff, and public. The subject will be further subdivided into fluoroscopy, radiography, and therapy, with emphasis upon the necessary safeguards of each application.

Course No. 31: Tuesday, 8:30–10:00 A.M.

Neuroradiology

ALFRED L. SCHMITZ, M.D.
San Francisco, Calif.

(*Continued from Monday, Course No. 23*)

Course No. 32: Wednesday, 8:30–10:00 A.M.

Bone Tumors

ROBERT D. MOSELEY, M.D.
Chicago, Ill.

Standard roentgenologic technics generally will differentiate neoplastic from non-neoplastic skeletal disease, and usually will distinguish benign from malignant lesions. In this discussion of bone tumors emphasis will be placed on accurate roentgenologic diagnosis based on familiarity with distinctive features. Despite efforts to evolve them and popular prejudices to the contrary, there are no fixed formulas for roentgen diagnosis of bone tumors. There are those cases which will elude the most subtle analysis. On the other hand, there are those conditions which are non-neoplastic and which confuse the radiologist by masquerading as neoplastic. In spite of these facts, it is possible to approach rationally the diagnosis of bone tumor. This rational radiologic approach is based on knowledge of the evolution and pathology of these lesions and on the interpretation of roentgen signs as reflecting the underlying pathologic changes.

(*This course continued Thursday, Course No. 40*)

Course No. 33: Wednesday, 8:30–10:00 A.M.

Radiation Exposure and Protection with Various Diagnostic Procedures

M. L. MEURK, B.A., and R. S. SHERMAN, M.D.
New York, N. Y.

A review of the radiation safety recommendations and requirements for diagnostic radiological installations will be presented, including methods for minimizing the dose to patients and to radiological personnel. The range of doses in various portions of the body, including the gonads, obtained with different diagnostic technics, will be discussed. These dose figures are obtained from measurements made by the instructors and those reported in the literature.

Course No. 34: Wednesday, 8:30–10:00 A.M.

Treatment Planning in Rotation Therapy

MORTON M. KLIGERMAN, M.D., and EDITH H. QUIMBY, Sc.D.
New York, N. Y.

Rotation therapy should not be considered as an isolated procedure, but rather as one of several technics to be investigated in planning treatment of any particular patient. The rotation process simply represents multiple-field cross-fire pushed to the limit. It is true that, by using a particular x-ray energy, it is usually possible to deliver to a centrally situated lesion a larger dose by rotation than by other technics. But it is not always possible to deliver an *adequate* dose.

As with any other treatment scheme, the principal factors determining its choice are (1) adequacy of tumor dose and (2) the differential between tumor dose and irradiation of healthy tissues. These will depend, among other things, on quality of radiation, target-axis distance, tumor size, body cross-section, type of tissue traversed, and beam definition. For instance, a small central tumor in the head can be treated adequately with 250-kvp x-rays, while a larger one in the pelvis requires more penetrating radiation.

Data will be given for a wide range of physical and anatomical factors, generalizations being drawn

REFRESHER COURSES

THE RADIOLOGICAL SOCIETY OF NORTH AMERICA

November 17 through November 22, 1957

PALMER HOUSE

CHICAGO, ILLINOIS

(Detach here) SEE INSTRUCTIONS ON REVERSE SIDE

FILL OUT THE FOLLOWING

(Print or type) .....

Last Name First Name or Initials

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Street Address

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City State

CHECK THE FOLLOWING

Member R.S.N.A. ☐ Guest ☐

Resident or fellow in Radiology at present ☐ Where .....

Medical Student ☐ Where .....

Reserve Officer on Active Duty at present ☐ Trainee in Physics ☐

Fill out, also, the enrollment diagram on the reverse side of this page

INSTRUCTIONS FOR ENROLLMENT

Read the accompanying description of the courses and plan of presentation. Register early; the number admitted to each course will be limited by the seating capacity of the rooms. Reservations will be made in the order of the receipt of request. Admission to the Refresher Course will be by badge and tickets except for Courses No. 1 and No. 7, when only a badge will be required. No tickets will be issued for these sessions.

Courses are limited to the medical profession, including graduate students and residents in radiology; radiation physicists, radiobiologists, chemists, and others closely concerned with the science of radiology; and medical students certified by the deans of their respective colleges.

You will note that this year a series of Refresher Courses has been added on Sunday afternoon; on Monday morning a second series has been added beginning at 10:30 a.m.

All tickets will be held for you at the R.S.N.A. Registration Desk in the Palmer House.

The registration fee, where applicable, will cover the cost of the Refresher Courses. Members, guest speakers, guest instructors, scientific exhibitors, residents or fellows in radiology, medical students, members of the Armed Forces, and trainees in physics do not pay a registration fee. Non-members not in these groups will pay, *at the time of registration*, a fee of $15.00, which will include the Refresher Courses.

PLEASE INDICATE YOUR FIRST, SECOND AND THIRD CHOICES

Tickets Will Be Picked Up at Time of Registration

	First Choice		Second Choice		Third Choice	
	Course No.	Instructor	Course No.	Instructor	Course No.	Instructor
Sunday, Nov. 17 4:30 P.M.						
Monday, Nov. 18 8:30 A.M.						
Monday, Nov. 18 10:30 A.M.						
Tuesday, Nov. 19						
Wednesday, Nov. 20						
Thursday, Nov. 21						
Friday, Nov. 22						

Mail this order sheet to John W. Walker, M.D., Chairman, Refresher Course Committee
Prior to Nov. 7, 830 Argyle Bldg., Kansas City 6, Mo.
After Nov. 7, c/o Radiological Society of North America, Palmer House, Chicago, Ill.

DO NOT SEND MONEY WITH THIS APPLICATION

as to their various fields of usefulness. Typical cases will be presented.

Course No. 35: Wednesday, 8:30–10:00 A.M.

The Small Intestine

RICHARD H. MARSHAK, M.D.
New York, N. Y.

(Continued from Tuesday, Course No. 27)

Course No. 36: Wednesday, 8:30–10:00 A.M.

Roentgen Cardiology

MELVIN M. FIGLEY, M.D.
Ann Arbor, Mich.

(Continued from Tuesday, Course No. 28)

Course No. 37: Wednesday, 8:30–10:00 A.M.

Diagnostic Applications of Radioactive Isotopes

H. L. FRIEDELL, M.D., and J. S. KROHMER, M.A.
Cleveland, Ohio

Various diagnostic uses of radioactive isotopes will be discussed, including clinical and physical criteria and requirements. Isotopes to be covered are I^{131} (iodine, serum albumin, rose bengal), P^{32}, Au^{198}, and Co^{60}.

Emphasis will be placed upon the following applications:

1. Thyroid function studies including uptakes, clearance rates, PBI's and TSH test.
2. Circulation studies, including blood volume, cardiac output, liver flow, and peripheral vascular studies.
3. Metabolic studies including pancreatic insufficiency studies and assay of "intrinsic factor."
4. Tumor localization including intraocular tumors.
5. Body scanning, including thyroid, liver, and blood pool.

Course No. 38: Wednesday, 8:30–10:00 A.M.

Irradiation Therapies for Carcinoma of the Urinary Bladder

J. R. MAXFIELD, JR., M.D.
Dallas, Texas

This course will seek to evaluate the different types of malignant change found in the urinary bladder, together with the choice of treatment best suited for the type of tumor and extent of involvement. An effort will be made to point out the merits and limitations of the various methods of irradiation. The excellent results with interstitial cobalt in nylon in certain infiltrating carcinomas of the bladder will be considered. Experience with these technics and impressions of the results achieved will be discussed.

Course No. 39: Wednesday, 8:30–10:00 A.M.

Dental Roentgenography

STANLEY A. LOVESTEDT, D.D.S.
Rochester, Minn.

This course will cover both odontogenic and systemic features which the physician-radiologist may encounter in intra- and extra-oral films. Cysts and other lesions of local origin will be presented, as well as the metabolic and developmental diseases which may give rise to changes in the teeth and supporting structures.

Course No. 40: Thursday, 8:30–10:00 A.M.

Bone Tumors

ROBERT D. MOSELEY, M.D.
Chicago, Ill.

(Continued from Wednesday, Course No. 32)

Course No. 41: Thursday, 8:30–10:00 A.M.

Dosage in Internal Use of Radium and Other Radioisotopes as Discrete Sources

ELIZABETH F. FOCHT, B.A.
New York, N. Y.

The principles and technics of dosage calculations in the use of discrete sources for intracavitary or interstitial therapy are similar for all gamma-emitting isotopes. This course will concentrate on discrete gamma sources, with emphasis as follows: The fundamentals of amount, exposure, filter, distribution, and resultant dose will be discussed for these sources in general. Different systems of radium-dosage evaluation and their recent modifications will be analyzed and adapted to the use of such isotopes as cobalt, gold, iridium, etc., including consideration of the time factor.

Three-dimensional models of some actual seed, needle, and tube distributions will be shown with their radiographs, and the processes of making them will be summarized. Methods of calculation from the radiographs or from the models will be explained.

An outline of the subject will be given with references, which should constitute a survey of information available—and philosophies—to date.

Course No. 42: Thursday, 8:30–10:00 A.M.

Some Fundamentals in Chest Roentgen Interpretation

BENJAMIN FELSON, M.D.
Cincinnati, Ohio

Chest roentgen interpretation should not merely represent an attempt to correlate particular shadows with specific diseases, but should be approached with an understanding of the basic principles of anatomy, physiology, pathology, and radiology involved. Some of these principles will be considered and their practical application illustrated.

Among the subjects to be discussed are:

Period I

1. A method of fluoroscopy
2. The "silhouette" sign
3. The air bronchogram

Period II

1. Anatomic variations in the pulmonary fissures
2. Lobar collapse
3. Lobar enlargement
4. The disrupted fissure

(*This course continued Friday, Course No. 49*)

Course No. 43: Thursday, 8:30–10:00 A.M.

Genetic Effects of Radiation

W. L. RUSSELL, Ph.D.
Oak Ridge, Tenn.

The following subjects will be considered: general information on genes and mutation; radiation-induced gene mutations and chromosomal aberrations, importance of the cell stage in gametogenesis at which mutations are induced; mutation rates in fruit fly, mouse and man; variation in mutation rates within a species; evidence that the genetic effects of radiation are cumulative; the shape of the curve for mutation rate and dose; comparison of spontaneous and radiation-induced mutations; the "rate-doubling dose" concept and its limitations; recessive and dominant mutations; the spectrum of effects of radiation-induced mutations; the high frequency of recessive lethal mutations and their time of killing; the increasing evidence of the importance of mutations with some dominant effects; the fate of mutations in the population; mutation, selection and evolution; recent evidence on damage in the first generation offspring of irradiated parents; summary of estimates of genetic hazards of radiation; the reports of the genetics committees of the U. S. National Academy of Sciences and the British Medical Research Council; the National Committee on Radiation Protection, the International Committee on Radiation Protection and the United Nations Scientific Committee; the research activities of the Atomic Energy Commission; general responsibility for controlling exposure to radiation; estimates of the gonad doses of radiation from various sources; the special responsibilities of the medical profession.

Course No. 44: Thursday, 8:30–10:00 A.M.

Roentgen Examination of the Sinuses and Mastoids

BARTON R. YOUNG, M.D.
Philadelphia, Penna.

The course will be given in two sessions. Discussion will be limited to the sinuses in the first period and to the mastoids in the second session. Technic of examination will be considered initially, and then normal and abnormal development from birth to maturity will be discussed and illustrated.

Roentgen findings in infections, tumors, and complications of chronic infections in the sinuses and mastoids, including mucoperiostitis, osteomyelitis, cholesteatoma, otogenic meningitis, and brain abscess, will be demonstrated. Several other interesting abnormalities will be included.

(*This course continued Friday, Course No. 51*)

Course No. 45: Thursday, 8:30–10:00 A.M.

The Statistical Point of View

HAROLD TIVEY, M.D.
Houston, Texas

The purpose of this course is to review, in a nonmathematical fashion, those statistical methods which are in current use or are available for evaluating the effects of therapy, or for the presentation of results of diagnostic studies.

Emphasis will be given to some logical and statistical pitfalls which combine to produce a well deserved skepticism of "statistics." Examples will be presented of some newer statistical methods which are more efficient for summarizing data, that is, which discard less hard-earned information than those now generally used. These methods will also produce a usable result of known reliability with shorter follow-up than the commonly employed technics.

This is a survey course, but notes and a bibliography will be supplied those interested in further study.

(*This course continued Friday, Course No. 52*)

Course No. 46: Thursday, 8:30–10:00 A.M.

Radiotherapy in Ophthalmology

GEORGE R. MERRIAM, JR., M.D.
New York, N. Y.

The use of radiation in the treatment of ocular lesions will be discussed, with particular attention paid to the late effects. The clinical course of various diseases will be described briefly and the anticipated benefits of irradiation evaluated in terms of other therapeutic measures and the possible late sequelae. The discussion will be divided into three categories: superficial, low-voltage, and high-voltage therapy. The factors, dose, treatment time, and technic for each condition will be considered.

Under *superficial therapy*, both grenz rays and beta radiation will be considered, and the treatment of such conditions as vernal catarrh, corneal vascularization, precancerous melanosis, recurrent pterygia, nodular episcleritis, phlyctenular keratitis, bullous and filamentary keratitis, and resistant corneal ulcers will be covered.

The *low-voltage therapy* discussion will concern primarily the treatment of epithelization of the anterior chamber. A brief discussion of the relative values of radiation and surgery in basal- and squamous-cell carcinomas of the lid will be presented.

Under *high-voltage therapy* such lesions as retinoblastoma, ocular lymphosarcoma, orbital hemangiomas, and metastatic carcinoma of the eye and orbit, will be covered.

Course No. 47: Friday, 8:30–10:00 A.M.

Aspects of Roentgen Therapy in Childhood

M. H. WITTENBORG, M.D.
Boston, Mass.

Most of the conditions amenable to radiotherapy will be mentioned during the period. The therapy of the common entities encountered in childhood will be discussed in a detailed manner.

Course No. 48: Friday, 8:30–10:00 A.M.

Useful Aids, Gadgets, and Appliances for X-Ray and Radium Therapy

JESSHILL LOVE, M.D.
Louisville, Ky.

A lantern slide presentation will show an interesting and useful collection of technics and gadgetry from several departments of radiotherapy. All of the material will be identified with the contributors.

Several devices, such as a home-made x-ray radiumionization chamber probe of small diameter, will be demonstrated. X-ray beam alignment and focal spots will be discussed. Audience participation will be invited at any time, and anyone may bring a 2 × 2-inch slide showing the application of a new or useful device. These slides will be collected and classified immediately prior to the course.

Course No. 49: Friday, 8:30–10:00 A.M.

Some Fundamentals in Chest Roentgen Interpretation

BENJAMIN FELSON, M.D.
Cincinnati, Ohio

(*Continued from Thursday, Course No. 42*)

Course No. 50: Friday, 8:30–10:00 A.M.

Fundamental Considerations in Radiation Biology

TITUS C. EVANS, Ph.D.
Iowa City, Iowa

The following topics will be considered:

1. Mechanisms of radiation injury as seen in the cell, the tissue, the organism and the offspring.
2. Variations in effects related to changes in quantity or quality of radiation.
3. Variation in radiosensitivity of tissues.
4. Modification of radiation reactions.
5. Effects of protraction and fractionation.
6. Aplasia and neoplasia.

Possible relationships of these biologic factors to certain problems in radiation therapy, protection, and public health will be discussed.

Course No. 51: Friday, 8:30–10:00 A.M.

Roentgen Examination of the Sinuses and Mastoids

BARTON R. YOUNG, M.D.
Philadelphia, Penna.

(*Continued from Thursday, Course No. 44*)

Course No. 52: Friday, 8:30–10:00 A.M.

The Statistical Point of View

HAROLD TIVEY, M.D.
Houston, Texas

(*Continued from Thursday, Course No. 45*)

Course No. 53: Friday, 8:30–10:00 A.M.

Radium Therapy

JOHN D. REEVES, M.D.
Boston, Mass.

Following an informal review of clinical and physical fundamentals in surface, interstitial, and intracavitary radium therapy, a variety of illustrative cases will be presented in brief detail with discussion of treatment and sample calculations of radium dosimetry. Examples of the usefulness of tantalum-182 wire, gold-198 grains, and cobalt-60 sources in "radium-substitute" therapy will be included. The usefulness of radium and cobalt in "bomb" form will be considered.

The comparative advantages and disadvantages of 400-kv to 2,000-kv x-ray therapy will be discussed in some cases.

An attempt will be made to interrelate some radiotherapeutic philosophies of Great Britain, Scandinavia, and Texas with some in this country.

Among other data, a progressive set of clinical radium problems, each covering one of the Paterson-Parker rules and with one method of solution, will be distributed. Discussion will be welcomed.

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THE HEAD AND NECK

Hypaque in Cerebral Angiography. A Clinical Assessment of Its Merits in Relation to Sodium Acetrizoate (Diaginol) and Diodone. A. T. Broadbridge. Brit. J. Radiol. **29**: 577–584, November 1956. (Atkinson Morley Hospital, Wimbledon, London, S. W. 20, England)

By comparing results with Diodone (35 per cent) and Diaginol (25 per cent) in roughly similar series of 100 consecutive cerebral arteriographic studies and Hypaque (25 per cent) in a series of 200 such examinations, the author attempted to determine which of the three media is to be preferred for this examination. Each substance was judged on the basis of the incidence of unsuccessful examinations, motion on the film due to the stimulus of the medium, the degree of opacity, carotid spasm, and the necessity for general anesthesia. Hypaque appeared to be the most satisfactory of the three media under this comparison.

Hypaque, 25 per cent, gave films of diagnostic contrast in 95 per cent of the cases. No increase in neurologic sequelae was noted with the use of 35 and 45 per cent solutions, though subjective complaints of warmth may increase. No serious sensitivity reactions were encountered.

Three roentgenograms; 4 tables.

G. M. Stevens, M.D.
Palo Alto, Calif.

The Use of Sodium Diacetrizoate in Cerebral Angiography. Jack Dunn, Jr., Alfred Uihlein, and Colin B. Holman. J. Neurosurg. **13**: 627–634, November 1956. (Mayo Clinic, Rochester, Minn.)

The authors consider the suitability of 50 per cent Hypaque (sodium diacetrizoate) for cerebral arteriography in a preliminary report based on 50 angiographic studies performed at the Mayo Clinic. There was no modification of their routine technic of carotid angiography except for the smaller amount of contrast medium required. Excellent visualization was obtained with only 3 to 5 c.c. of Hypaque in single injections. A complete examination could be performed with as little as 16 to 20 c.c. of Hypaque, as compared to 50 to 60 c.c. of Diodrast.

No serious complications were encountered other than rather extensive homolateral petechial hemorrhages involving the face and neck on the side of injection, in 2 patients. These disappeared in about three days. In no case was there development of hemiplegia or hemiparesis.

Nine roentgenograms; 1 photograph.

Charles M. Greenwald, M.D.
Iowa City, Iowa

Safe Angiography. J. N. Segelov. J. Neurosurg. **13**: 567–574, November 1956. (% Bank of New South Wales, Berkeley Square, London W. 1, England)

The author reviews the results of 660 angiographic studies performed on 400 patients at the Royal Prince Alfred Hospital, Sydney, Australia. Diodrast 35 per cent was used for the first 300 angiograms, and sodium acetrizoate (Diaginol) 30 per cent for the remainder. A percutaneous technic of injection was employed, and only 8 c.c. of contrast agent was given per view. The technic is described and the diagnostic value of the procedure in varying conditions is discussed.

In this series there were no deaths, no permanent sequelae, nor any transient complications except for a cutaneous rash in 1 per cent of cases. This absence of complications is attributed to the small volume of contrast agent used, careful individualized premedication and choice of anesthetic, and to the repeated use of the technic described.

Six tables.

Charles M. Greenwald, M.D.
Iowa City, Iowa

The Results of Surgical Treatment of Intracranial Aneurysms as Demonstrated by Progress Arteriography. Lester A. Mount and Juan M. Taveras. J. Neurosurg. **13**: 618–626, November 1956. (J. M. T., Department of Radiology, Columbia University College of Physicians and Surgeons, New York 32, N. Y.)

The authors discuss the results of surgical therapy in 51 cases of intracranial aneurysm, as shown by 54 progress arteriograms. Although the series is considered too small for conclusions on a statistical basis, certain inferences are made: (1) Arteriographically the results of direct surgical attack on the aneurysm were better than those of any form of carotid ligation. (2) The results of complete and permanent ligation of the internal or common carotid were better than partial or temporary ligation. Of these two, ligation of the internal carotid was superior. (3) Ligation of the carotid arteries in the neck using a tantalum clip was likely not to be complete and permanent, as in 6 of 8 cases the clip was found to be open. (4) There were only 2 patients in the entire treated group in whom the aneurysm was larger. In both of these the clamp or clips were found to be open, emphasizing the importance of complete ligation.

There were no complications as a result of the progress arteriograms, except for a temporary paresis of an extremity in 1 patient.

Progress arteriography is not considered a completely definitive method of evaluating results, especially in patients with larger aneurysms. The clinical signs and symptoms must be considered, as occasionally the aneurysm will fail to visualize even though complete ligation has not been achieved. One obvious explanation is that the aneurysmal sac may be filled with clotted blood.

In a control group of 16 patients with aneurysms untreated by surgery, progress arteriograms demonstrated the aneurysm in all instances; in 13 it was unchanged in size and in 3 it was larger.

Five roentgenograms; 4 tables.

Charles M. Greenwald, M.D.
Iowa City, Iowa

Infarctions Simulating Brain Tumors in the Posterior Fossa. Sten O. Lindgren. J. Neurosurg. **13**: 575–581, November 1956. (Sahlgrenska Sjukhuset, Göteborg, Sweden)

Occlusion of the cerebral arteries may cause circulatory disturbances in the involved area resulting not only in malacia and atrophy, but also in temporary edema with increased pressure and tumor symptoms. This is best known with respect to occlusions of the internal carotid and its branches.

The author reports 2 cases of vascular occlusion presenting the clinical and roentgenological picture of posterior fossa tumors. At operation softening in a cerebellar hemisphere with increased intracranial pressure was found. Autopsy in 1 case revealed a thrombosis of the corresponding vertebral and posterior inferior cerebellar artery. In the other patient an irregular narrowing of the vertebral artery was demonstrated by postoperative angiography.

The variation in vascular supply to the posterior fossa area is discussed. Classical occlusion of the posterior inferior cerebellar artery usually gives rise to softening of the lateral medulla, but involvement of the cerebellar hemispheres is not usually reported. Surgical intervention is indicated when infarction in the posterior fossa gives rise to increased intracranial pressure.

Four roentgenograms; 1 drawing.

CHARLES M. GREENWALD, M.D.
Iowa City, Iowa

Communicating Hydrocephalus from Subarachnoid Bleeding. Eldon L. Foltz and Arthur A. Ward, Jr. J. Neurosurg. **13:** 546–566, November 1956. (Division of Neurosurgery, University of Washington, Seattle, Wash.)

The authors present 10 cases in which subarachnoid bleeding was followed by communicating hydrocephalus. Such delayed progressive obstruction of the cerebrospinal pathways of the cisterns at the base of the brain, resulting in severe, crippling neurological defects and possible fatality, has not been widely recognized as a complication of massive hemorrhage.

In this series, 2 cases were due to operative hemorrhage, 5 to rupture of an intracranial aneurysm, and 3 to head trauma. It is postulated that liquefication and absorption of the clotted blood evokes an inflammatory response with secondary adhesive arachnoiditis of the basal leptomeninges.

The interval between the occurrence of bleeding and recognition of hydrocephalus ranged from two to twelve weeks. The signs and symptoms are variable and may easily be ascribed to non-specific delayed effects of the original lesion producing hemorrhage. In none of the authors' cases was the diagnosis of progressing communicating hydrocephalus made until the condition was demonstrated by pneumoencephalography. Treatment by ventriculomastoid shunt operations resulted in marked clinical improvement in 6 cases, impending fatality being averted in 3 of these.

These observations concerning communicating hydrocephalus in adults have led the authors to speculate regarding the genesis of so-called idiopathic communicating hydrocephalus of infancy. The possible role of an adhesive arachnoiditis secondary to subarachnoid bleeding from birth trauma and moulding of the head is briefly discussed.

Eighteen roentgenograms; 2 tables.

CHARLES M. GREENWALD, M.D.
Iowa City, Iowa

An Appraisal of Pneumoencephalography in Mental Retardation and Epilepsy. Leon I. Charash and Henry S. Dunning. Pediatrics **18:** 716–720, November 1956. (L. I. C., 525 E. 68th St., New York 21, N. Y.)

Following a brief historical summary, the authors analyze 151 encephalograms obtained on the Pediatric Service of the New York Hospital from 1938 through 1954. One hundred and six patients were mentally deficient at the time of examination. In this group, correlation between the degree of retardation found by psychometric examinations and the encephalogram was poor. Thus, in 25 of the most retarded children air studies were normal and 2 patients with marked cerebral atrophy were later noted to have normal intelligence. Of 45 patients with idiopathic epilepsy studied by this method, 33 showed normal findings, 7 slight cerebral atrophy, and 1 a porencephalic cyst; in 4 the examination was unsuccessful.

There were 2 deaths, 9 major complications, and 41 minor side effects as a result of the 151 air studies. It would appear from an analysis of these cases and a critical survey of the literature, as well as cognizance of the hazards involved, that the information yield in mental retardation and "idiopathic" epilepsy does not warrant pneumoencephalography. The authors recommend that the procedure be abandoned as a diagnostic tool in the study of these two conditions.

Two tables.

SAUL SCHEFF, M.D.
Boston, Mass.

THE CHEST

Bronchial and Arterial Anomalies with Drainage of the Right Lung into the Inferior Vena Cava. Nicholas A. Halasz, Katherine H. Halloran, and Averill A. Liebow. Circulation **14:** 826–846, November 1956. (N. A. H., Yale University School of Medicine, New Haven, Conn.)

Total venous drainage of the right lung into the inferior vena cava is reported in 3 cases, and the literature covering 18 similar observations is reviewed. In each of the authors' cases and in some of those from the literature associated bronchial anomalies were found. In the present investigation bronchial and vascular casts were made from the surgical specimens for the purpose of better studying the nature and extent of these anomalies.

On radiographic examination the right hemithorax often appears smaller than the left. The right auricle, pulmonary artery segment, and left branch of the pulmonary artery show undue fullness. Sometimes the anomalous vessel can be seen, appearing as a dagger- or scimitar-shaped band of increased density pointing upward and slightly outward along the right heart border. This appearance is quite characteristic, and the authors believe it should at once suggest the diagnosis.

Angiocardiography reveals right heart enlargement. Opacification of the anomalous right paracardiac vessel and the left pulmonary veins occurs simultaneously. Bronchograms demonstrate whatever anomalies may exist in the distribution of the bronchi, and occasionally show the presence of cystic diverticula of the bronchial tree.

Knowledge of these anomalies and diverticula is significant in the planning and execution of surgery.

Twenty-eight figures; 1 table.

DON E. MATTHIESEN, M.D.
Phoenix, Ariz.

Farmer's Lung in Radnor and North Breconshire. A Report of Ten Cases. D. Ivor Williams and P. P. Mulhall. Brit. M. J. **2:** 1216–1218, Nov. 24, 1956. (Brecon Chest Clinic, Brecknock, Breconshire, Wales)

"Farmer's lung" is an acute or subacute respiratory illness developing after exposure to mouldy hay. Ten

additional cases are reported, all seen within four months in a relatively small area in mid Wales. This minor epidemic occurred in the early part of the year, when stored hay is old, dusty, and likely to have developed moulds, especially if not properly dried before storing. An exposure history was obtained in all cases. Clinical features included marked dyspnea on exertion, usually associated with cough with or without expectoration. In all instances the radiographs showed a fine, diffuse mottling of the lung fields confined mainly to the middle and lower zones. Clinical improvement occurred rapidly after cessation of contact with the hay dust, but at least three months elapsed before clearing of the radiographic changes. Proper therapy (besides removal from the irritating hay dust) consists in large doses of potassium iodide, and a prompt response to this medication tended to confirm the diagnosis.

The chief condition to be considered in the differential diagnosis is miliary tuberculosis. The finding of bacilli in the sputum with staining characteristics similar to those of the tubercle bacillus adds to the difficulties of differentiation. Sputum culture for the *M. tuberculosis* is the important differential point. Bacteriological and fungus studies of the offending hay did not show good correlation with cultures obtained from the patients' sputa.

The authors feel that the presence of moulds in the hay is an essential feature for the infection, but that some individual susceptibility must also exist.

Findings in the 10 reported cases are given in tabular form. Three cases with somewhat atypical histories are further detailed.

Two tables.

JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Catheter Migration from Uterus to Lung, Perforating the Diaphragm. A Case Report. Mary M. Powell. Dis. of Chest. **30:** 583–584, November 1956. (Johns Hopkins Hospital, Baltimore, Md.)

The author reports the case of a 31-year-old white woman with symptoms suggestive of lung abscess. At thoracotomy an encrusted catheter 12 inches long was found in the left chest, extending from below the diaphragm to the left upper lobe and necessitating left upper lobectomy. On postoperative questioning, the patient stated that she had undergone a criminal abortion one year earlier.

Two roentgenograms.

Malignant Thymoma (Lymphocytic Type). James I. Hudson, Jr., Francis P. Catanzaro, A. F. Bloodworth, and O. W. Topp. J. Pediat. **49:** 197–201, August 1956. (U. S. Air Force Hospital, Lake Charles Air Force Base, Lake Charles, La.)

Mediastinal tumors are not often considered in the differential diagnosis of atelectasis and pneumothorax. The authors report the case of a 4-year-old white boy with a large malignant thymoma which in its position, size, and x-ray appearance mimicked a bilateral partial atelectasis with pneumothorax. The clinical picture was further confused by the occurrence of marked cyanosis and orthopnea. The diagnosis was made only after the patient's death, during an attempt to massage the heart. The tumor surrounded and involved the aorta and great vessels, the pericardium, and the hilus of the lung, but did not show the eccentric enlargement characteristic of mediastinal tumors. There was no associated myasthenia gravis.

When strict diagnostic criteria are observed, thymic cancer proves to be of infrequent occurrence. Morgan and Dudley (New England J. Med. **253:** 625, 1955) found a total of 44 cases in the literature which appeared to fit the pathologic criteria of invasiveness and cellular type.

Three roentgenograms; 1 photograph.

THE HEART AND BLOOD VESSELS

The Angiocardiographic Pattern of High Ventricular Septal Defect with Left to Right Shunt. Louis A. Soloff and Jacob Zatuchni. Am. J. M. Sc. **232:** 528–532, November 1956. (Temple University School of Medicine and Hospital, Philadelphia, Penna.)

An instance of high ventricular septal defect with left-to-right shunt is described to illustrate the pathognomonic angiocardiographic pattern of this defect. This pattern is described as consisting of "a rapid intracardiac circulation time and a rapid right heart time followed by reopacification of the outflow tract of the right ventricle contiguous with an immediately preceding opacified left ventricle. The opacification of the left ventricle, outflow tract of the right ventricle, pulmonary artery and aorta are all prolonged. The pulmonary artery and its branches are disproportionately enlarged. The left and right ventricle as well as the left atrium may be enlarged."

Reopacification of the right ventricle, the indispensable angiocardiographic finding, can be demonstrated with certainty only if the right ventricle shows little or no opacification when opacified blood from the left ventricle first begins to pass through the defect. This demonstration is facilitated by exposing roentgenograms at right angles to the shunt.

Although the greater portion of the ventricular septum is tangential to the frontal plane, its cranial portion, the site of almost all ventricular septal defects, is virtually parallel to it. The lateral projection is, therefore, the one of choice. This projection also permits maximal separation of the significant outflow tract of the right ventricle from the left. In the authors' experience, this projection is also best for minimizing overlapping by the opacified chambers of the left heart, great vessels, and even by the spine. However, an additional projection is necessary to recognize change in opacity due to depth alone.

One angiocardiogram; 2 diagrams.

ALFRED O. MILLER, M.D.
Louisville, Ky.

Diagnosis of Mitral Regurgitation by Cardioangiography. Philip W. Smith, Hugh A. Cregg, and Karl P. Klassen. Circulation **14:** 847–853, November 1956. (P. W. S., Frederick C. Smith Clinic, Marion, Ohio)

For the preoperative radiographic differentiation of mitral stenosis and mitral insufficiency, the authors have found very useful the direct intracardiac injection of a contrast medium into the left ventricle. This article describes their technic and reviews their experiences with 20 patients so studied.

The procedure appears relatively simple and safe, and has permitted fairly good assessment of the state of competence of the mitral valve. In 6 cases of the series, surgical or autopsy evidence was available for comparison with cardioangiographic findings, and in 5 of these there was good agreement. In 10 cases the mitral valve was found to be entirely competent with no

opacification of the left auricle on serial films. In 10 cases mitral regurgitation of varying degrees was demonstrated by increased opacity of the left atrial region. In the 1 case where surgical and cardioangiographic findings were not in agreement, the surgeons found stenosis and regurgitation, though the valve appeared competent radiographically.

Eight roentgenograms; 2 photographs.

DON E. MATTHIESEN, M.D.
Phoenix, Ariz.

Stratigraphy in the Diagnosis of Mitral Disease. Ciro Sandomenico. Radiol. med. **42:** 1076–1085, November 1956. (In Italian) (Università di Napoli, Naples, Italy)

In cases of mitral disease, body-section roentgenography, in frontal and/or right anterior oblique projection, may reveal the size and shape of the enlarged left atrium, and at times even of its auricular appendage. When present, deformity of the tracheobronchial bifurcation is also seen. In addition, the azygos and the right middle and lower pulmonary veins are visualized, which allows a gross evaluation of the status of the pulmonary circulation and thus permits a certain degree of clinical correlation. The use of planigraphy in heart disease (of both rheumatic and other origins) deserves encouragement.

Thirteen roentgenograms. E. R. N. GRIGG, M.D.
Cook County Hospital, Chicago

Calcification of the Pericardium Caused by a Hitherto Unrecognized Etiological Factor. Morris Kleinfeld and Charles P. Giel. Am. Heart J. **52:** 899–904, December 1956. (Division of Industrial Hygiene, New York State Department of Labor, New York, N. Y.)

In a recent clinico-roentgenographic study of workers employed in talc mills and mines (Kleinfeld et al: Arch. Indust. Health **12:** 66, 1955. Abst. in Radiology **66:** 781, 1956), 3 examples of calcification of the pericardium were observed. Brief histories of these cases are given. In all there was a long exposure to talc dust, twenty-four, forty-seven, and thirty-four years respectively. In one case calcification was known to have been present for five years, and in a second for fifteen years. In all 3 cases the pericardial calcification persisted without significant changes in cardiac size or evidence of disturbed hemodynamics. There was no history of chest trauma, unexplained or prolonged fever, hypertension, rheumatic fever, or tuberculosis. The clinical course was that of slowly progressive pulmonary dysfunction due to talc pneumonoconiosis, with no evidences of cardiac failure.

The presence of calcification in the diaphragmatic pleura is a frequent occurrence in talc workers. This favors a similar etiology for the calcification of the pericardium. The exact mechanism is not known. The authors believe it is best explained by a mechanical effect of the talc fibers on the pericardium, causing a chronic inflammatory response and increased capillary hemorrhage with subsequent deposition of calcium.

Six roentgenograms. HENRY K. TAYLOR, M.D.
New York, N. Y.

A Technique of Abdominal Aortography and Femoral Arteriography. Charles V. Menendez and Robert R. Linton. Surgery **40:** 718–736, October 1956. (Massachusetts General Hospital, Boston 14, Mass.)

A simple technic is outlined for obtaining translumbar aortograms with simultaneous bilateral femoral arteriograms, and individual percutaneous femoral arteriograms. No elaborate apparatus or special teamwork is required, and the procedure can be carried out in the smallest hospital. Two prolonged exposures of 2.5 seconds each are the chief feature of the method. The authors' personal experiences with approximately 350 aortograms and arteriograms form the basis for this report. The importance of a circulation-time test prior to percutaneous femoral arteriography is emphasized. The incidence of complications has been remarkably low.

In an addendum, the authors report one anesthesia death from cardiac arrest following aortography. All aortographic examinations performed under Thiopental anesthesia are now carried out in the operating room with an inlying endotracheal tube and an intravenous muscle relaxant. The technic, as described in the body of the article, has been modified for operating room cases. Three-second exposures are employed for both films.

At the time of publication, 595 aortograms and femoral arteriograms had been taken, with the death mentioned above as the only serious complication. Sixty-one aortograms were obtained without femoral arteriograms and 85 aortograms with 158 simultaneous femoral arteriograms of either one or both extremities. Two hundred and ninety-one femoral arteriographic examinations had been made by the percutaneous route.

Fifteen roentgenograms; 3 photographs; 4 tables.

Dissection of Aorta as a Complication of Translumbar Aortography. H. Gaylis and J. W. Laws. Brit. M. J. **2:** 1141–1146, Nov. 17, 1956. (Postgraduate Medical School of London, London, England)

The authors describe a complication of lumbar aortography in which a part or all of the contrast substance is injected into the media of the aorta, causing a dissection of that vessel analogous to a spontaneous dissecting aneurysm and giving rise to a characteristic x-ray picture. This event may lead to misinterpretation in diagnosis if its true significance is not appreciated; it may produce serious sequelae; and it may occur in spite of the most scrupulous technic. It is believed to be not uncommon and to offer an explanation for some of the complications of aortography usually ascribed to arterial thrombosis or to the direct toxic effect of the contrast medium.

Two cases are described in which lumbar aortograms were obtained showing a picture superficially resembling iliac thrombosis. This diagnosis, however, was incompatible with the clinical features, and the authors were "forced to the conclusion"that the unusual appearances had been produced by some form of "extravasation," probably an intramural injection of contrast medium. In a further study of this phenomenon, they incorporated a number of human aortas from fresh cadavers into the circuit of a Melrose heart-lung machine. It was found that the wall of the aorta could be easily separated into two layers by gentle blunt dissection or intramural injection of saline. The plane of cleavage appeared to be adjacent to the intima.

The factors contributing to intramural injection of the contrast substance and some safeguards against this complication are discussed.

Comments on this paper appeared in the Correspondence columns of the *British Medical Journal* for

Jan. 26, 1957 (p. 225) and Feb. 9 (p. 340). David Sutton, in the first of these, criticizes the technic employed by Gaylis and Laws which he feels does not include adequate precautions against the mishap which they describe and calls for excessive doses of the medium (30 to 40 ml. of 70 per cent Diodone). He makes use of a test-dose method to localize the needle point during aortography and on several occasions has thus avoided injection of the whole quantity of contrast material directly into a renal artery or other major branch of the aorta. He emphasizes the direct toxic effect of the medium on the nervous system, and points out that the needle itself can traumatize an artery.

R. E. Horton and F. G. M. Ross, in the later communication, express their agreement with Sutton that lower concentrations of the contrast medium are desirable. They believe that a medium of high concentration should never be injected into the vascular system anywhere if one of lower concentration will give diagnostic radiographs. They consider it doubtful if aortography should be employed except in disease of the aorta or great intra-abdominal arteries of such a nature that direct surgery is contemplated and will be made easier by radiographic delineation of the disease.

Massive Thrombotic Occlusion of the Large Pulmonary Arteries. K. P. Ball, J. F. Goodwin, and C. V. Harrison. Circulation **14:** 766–783, November 1956. (K. P. B., Central Middlesex Hospital, London, England)

The authors review 23 cases of massive thrombotic occlusion of the large pulmonary arteries, 9 of which were seen during life, while 14 were obtained from autopsy records. Four cases are reported in full; pertinent details of the remainder are presented in tabular form.

In about one-third of the series there was primary thrombosis formation *in situ*, while the remainder were thought to be secondary to pulmonary embolism. Associated diseases were chronic bronchitis, lung cancer, coronary artery disease, congenital heart disease, and valvular heart disease. In 3 cases there was a generalized thrombo-embolic tendency of unknown etiology. The thrombi evidently developed on a basis of atherosclerosis, low cardiac output, sluggish pulmonary blood flow, and enlargement of the main pulmonary arteries.

Large, poorly pulsating main pulmonary arteries with small, underfilled peripheral lung vessels were the most important roentgenologic sign in these cases. Pulmonary infarcts sometimes produced shadows in the clear lung fields. Right heart enlargement and fullness of the pulmonary artery segment were more or less constant findings. The point is made that cases of pulmonary stenosis may cause confusing enlargement of the main pulmonary arteries with diminished pulsations. Differentiation from mitral stenosis was at times aided by the radiologic demonstration of left auricular enlargement in mitral disease, as contrasted with the right heart enlargment associated with massive thrombi of the main pulmonary arteries.

Sometimes thrombosis of large pulmonary arteries occurs insidiously, producing a clinical and radiologic picture of progressive right ventricular failure. In these cases, the low heart output not only causes reduction of pulmonary vascular pulsations and clear lung fields, but also produces symptoms of diminished coronary and cerebral blood flow. The disease should be suspected when patients with mitral disease begin to deteriorate for no apparent reason and show decreased pulmonary artery pulsations.

Treatment with anticoagulants may be helpful if the diagnosis can be made early.

Ten figures; 4 tables. DON E. MATTHIESEN, M.D.
Phoenix, Ariz.

Portal Hypertension in a Child Diagnosed by Splenoportogram. Ahmed I. Kirimli, Ali Ertugrul, and Samuel Levine. J. Pediat. **49:** 177–184, August 1956. (Albert Einstein Medical Center, Northern Division, Philadelphia, Penna.)

The authors report the case of a 3-year-old girl in whom a cavernous transformation of the portal vein was diagnosed by splenoportogram. Splenography was repeated at laparotomy and the results duplicated. Ligation of the splenic artery did not prove helpful; portal hypertension was not relieved, nor was the blood picture changed. A splenorenal shunt was later attempted, but could not be done because of the small size of the veins. Splenectomy and ligation of the varices were carried out, after which the child's blood picture and general condition improved.

If upper gastrointestinal x-ray studies suggest varices of the esophagus or cardia, splenoportography should be performed so that the splenic and portal veins can be well defined. This is a helpful procedure in all cases of portal hypertension in that it gives a direct means of differentiating the many causes of portal block, intra- or extra-hepatic. Since hemorrhagic diathesis is a contraindication to splenography, prothrombin determination should precede the examination. A preliminary film should be taken to determine the size of the spleen. Urokon 70 per cent or Diodrast is used, and exposures are started when three-quarters of the medium has been injected. Optimum results may be anticipated with use of a rapid cassette changer, preferably one electrically controlled. Varicosities in the esophagus and the cardiac end of the stomach are depicted clearly. Very large varicosities at the cardia may be differentiated from possible tumors.

Five roentgenograms; 3 photographs; 1 chart.

THE DIGESTIVE SYSTEM

Oesophageal Atresia with a Review of Twelve Cases. Martin Spiro. Brit. J. Radiol. **29:** 514–516, September 1956. (West Middlesex Hospital, Isleworth, Middlesex, England)

Contrary to the earlier view, esophageal atresia is now recognized as one of the commonest conditions requiring surgical treatment in the neonatal period. At least 90 per cent of the cases are associated with tracheoesophageal fistula. Coexistent extra-esophageal congenital defects are to be expected, having been found in 63 and 87 per cent, respectively, of two reported series (Plass: Johns Hopkins Hosp. Bull. **18:** 259, 1919; Ladd: New England J. Med. **230:** 625, 1944. Abst. in Radiology **44:** 94, 1945).

Examination consists in preliminary passage of a catheter into the esophagus to determine the presence of obstruction, roentgenography of the chest and abdomen, and fluoroscopy following the introduction of a small amount of iodized oil through an esophageal catheter. Survey films should be studied for any concurrent congenital anomalies.

A lateral chest film may show anterior displacement

of the trachea, as well as posterior compression of its posterior border. This sign was reported by Holt *et al.* in 60 per cent of 40 cases for which lateral views were available (Radiology **47**: 457, 1946).

Twelve cases seen in the West Middlesex Hospital over a twelve-year period are reviewed.

Two roentgenograms.

PAUL W. MATHEWS, JR., M.D.
Bowman Gray School of Medicine

Gastric Varices: Characteristics and Clinical Significance. Bernard H. Smookler. Gastroenterology **31**: 581–587, November 1956. (1139 Gould Road, Lansing, Mich.)

Although it is well known that portal hypertension may result in esophageal varices, little attention has been directed to the related but less common formation of gastric varices. Any obstruction to portal or splenic flow of blood, such as that due to cirrhosis, tumors, or thrombosis, would tend to produce varices in the gastric fundus. Rarely varices may occur as a congenital anomaly. Generalized angiomatosis is another possible cause. Most commonly, however, they are the result of cirrhosis.

Radiologically, most cases are found around the cardia or occasionally in the fundus. The lesions measure about 1-2 cm. in diameter and are seen as smooth rounded masses which protrude into the lumen. In the absence of associated esophageal varices, differentiation from carcinoma is often difficult. Lesions grouped about the esophageal orifice without evidence of obstruction or involvement of the abdominal portion of the esophagus, and with the presence of an enlarged spleen, are more suggestive of varices than carcinoma.

The following roentgen criteria, demonstrable on films taken with the patient in the supine left oblique position after the ingestion of barium and air contrast, were suggested by Samuel (Brit. J. Radiol. **21**: 519, 1948): (1) thick, tortuous mucosal folds of a polypoid nature located over the greater curvature and extending up into the cardia; (2) distortion of the mucosal pattern by the presence of round, clear areas giving the appearance of bubbles; (3) the presence of esophageal varices; (4) an enlarged spleen compressing the fundus.

The author reports a case in a 71-year-old patient with chronic alcoholism and liver cirrhosis. Roentgenograms showed a polypoid lesion at the posterior aspect of the gastric cardia without ulceration. Esophageal varices and an enlarged spleen were not seen. Gastroscopy revealed an elevated, well circumscribed, non-pulsating, pale, granular mass, with surface petechiae, at the fundic portion of the greater curvature. At operation there was evidence of cirrhosis, portal hypertension, and large tortuous veins in the falciform ligament. The splenic vein and artery were dilated and tortuous. Manipulation of the lesion during surgery produced massive bleeding. Although hemostasis was successful, severe hemorrhage again occurred on the fourteenth postoperative day, with death on the following day. At autopsy the mass was found to be a varix arising from the dilated left gastroepiploic vein, which joined a dilated splenic vein. A thrombus was present at the junction of the left gastroepiploic vein and the splenic vein. The primary etiologic factor in the production of the varix was thought to be portal hypertension. The splenic thrombus apparently contributed to the venous backflow.

The diagnosis of gastric varices should be entertained in cases showing defects in the upper stomach. Recognition of the condition may explain otherwise obscure gastric bleeding.

One roentgenogram.

MORTIMER R. CAMIEL, M.D.
Brooklyn, N. Y.

Radiological Demonstration of Gas in the Stomach Wall. K. Lumsden. Brit. J. Radiol. **29**: 596–600, November 1956. (Radiological Department, United Oxford Hospitals, Oxford, England)

The author reports a case in which gas was radiographically demonstrable in the stomach wall of an 83-year-old male suffering from an obstructing neoplasm (presumably carcinoma) of the pylorus. It is supposed that a bout of vomiting may have forced air from the lumen of the stomach into the wall (possibly through ulceration in the pyloric tumor).

There are three conditions in which gas may be found in the stomach wall: (1) emphysematous gastritis, caused by a gas-forming organism; (2) cystic pneumatosis, a localized collection of tiny cysts in the submucosa or subserosa, of unknown etiology; (3) interstitial gastric emphysema. The case reported here belongs in the third group. Such cases are usually incident to the performance of gastroscopy. Their spontaneous occurrence appears to be very rare. The author was able to find but one other example in which the diagnosis was made in a living subject who had not been examined gastroscopically, but in that case there had been an unsuccessful attempt at intubation (Cancelmo: Radiology **63**: 81, 1954).

Four roentgenograms.

G. M. STEVENS, M.D.
Palo Alto, Calif.

Transpyloric Mucosal Prolapse. A. Frank. Fortschr. a. d. Geb. d. Röntgenstrahlen **85**: 534–543, November 1956. (In German) (Mariahilferstr. 1d, Vienna 6, Austria)

The existence of true mucosal prolapse has been frequently questioned in the European literature of recent years but, in spite of all arguments against the entity, the author believes that such a prolapse actually occurs. His pathologic material consisted of 1,328 autopsy and 178 surgical specimens. The diagnosis of mucosal prolapse could be made in 9 cases, or 0.59 per cent. In one of these the condition had been recognized roentgenologically shortly before death. This case is described and illustrated. Symptoms existed in only 3 of the other 8 cases.

Roentgenologic diagnosis of true prolapse is valid only on films obtained in orthograde projection. A prolapse can easily be simulated in the oblique view when a so-called portio duodenalis pylori causes an impression or indentation of the base of the bulb. Pathologically, the occurrence of fat tissue in the submucosal layer of the prolapsed portion is believed to be fairly characteristic.

Clinically, there are no specific findings, but in cases with nausea and vomiting the symptoms can be ascribed to the prolapse if no other lesions are found. In asymptomatic cases, however, the proper evaluation of positive roentgen findings is possible only in conjunction with the clinical impression.

The author found prolapse in 1.4 per cent of all gastrointestinal examinations. While this is a lower figure than has been reported by others, it is still more than twice that for pathologic material. The relatively low incidence is attributed to stricter diagnostic criteria, with elimination of oblique projections and of pyloric

ring protrusions. The fact that prolapse is observed more often roentgenologically than pathologically is believed to be due to its transient nature in some cases.

The author has made the roentgen diagnosis of prolapse in 26 non-verified cases. Of these 18 were symptomatic and 8 asymptomatic. Four cases are briefly reported and illustrated.

Six roentgenograms, 2 photographs, 1 photomicrograph, 3 drawings; 1 table. ERNEST KRAFT, M.D.
Northport, N. Y.

The Problem of Absent or Deficient Gas Pattern in the Intestines in Early Infancy. S. B. Feinberg, A. R. Margulis, and C. M. Nice. Pediatrics **18:** 790–798, November 1956. (Department of Radiology, University of Minnesota, Minneapolis 14, Minn.)

The authors cite a variety of conditions in infants associated with a deficient intestinal gas pattern. These they classify as follows: (1) interference with normal transport due to respiratory distress in the newborn, (2) mechanical obstruction, (3) associated mechanical and dehydration mechanisms, and (4) unrelated causes of dehydration.

(1) In a review of the films of 65 newborn and young infants in severe respiratory distress from a variety of causes, only 6 showed absence or diminution of intestinal gas; in 17, however, there was a deficiency of the expected gas pattern in the intestines. The common mechanism in these cases is a temporary disturbance in normal swallowing accompanying the dyspnea.

(2) The various congenital conditions causing mechanical obstruction, such as atresia, diaphragms, stenosis, malrotation with volvulus, bands, and extrinsic compression by anomalous structures, lead to more or less characteristic gas patterns as seen on the roentgenogram. In many of the infants in this group the picture is indistinguishable from those obtained in the absence of mechanical obstruction.

(3) The relation of dehydration to the small intestinal gas pattern was studied in 40 proved cases of hypertrophic pyloric stenosis and the conclusion was reached that the gas pattern is not entirely a function of the degree of hypertrophy but is largely dependent on the extent of concomitant hydration. In general, the severer the dehydration the more likely the absence of a gas pattern and an associated elevated carbon-dioxide combining power. The converse appears to be true, the better the infant's state of hydration the less likely it is to show a deficiency of the intestinal gas pattern. Restoration of hydration in the few cases in which it was undertaken was followed by a striking increase in small intestinal gas, further indicating that the mechanical factor is not entirely responsible for the deficiency.

One dehydrated patient showed an absence of intestinal gas following repair of a tracheoesophageal fistula despite a patent esophagus. Another, with evidence of an obstruction at the ligament of Treitz, was found at operation to have only a hypoplastic intestine with neuromuscular dysfunction.

(4) Although abdominal distention is the usual finding in infants with diarrhea, in the severe case, with dehydration, there will be a paucity of gas due to the collapse of the intestinal lumen. Adrenal insufficiency, with vomiting and diarrhea leading to dehydration, may produce an abdominal film indistinguishable from that of pyloric stenosis.

There would appear to be more than a coincidental relationship of hydration, electrolyte imbalance, and intestinal gas pattern.

Thirteen roentgenograms; 1 table.
SAUL SCHEFF, M.D.
Boston, Mass.

Collagen Disease of the Small Bowel. Irving Marshall. New England J. Med. **255:** 978–983, Nov. 22, 1956. (1905 Hudson Blvd., Jersey City, N. J.)

Three cases are reported, illustrating various features of collagen disease involving the small intestine.

The first patient was a 47-year-old male with initial complaints and findings suggesting a primary neoplasm of the distal duodenum. At surgery the appearance of the intestine (edema, flabby tone, moderate distention, soft regional lymph nodes) indicated a diagnosis of regional enteritis, so that definitive surgery was not undertaken. Because of repeated bouts of digestive disturbance and a steadily downhill course, a second operation was performed about nine months after the first. At this time the appearance of the involved bowel, which extended from the mid-duodenum into the proximal ileum, had changed. The wall was now thin and flabby, with scattered areas of dilatation and absence of peristalsis. Lymph nodes were firm and small and showed radiating channels filled with a whitish substance. A long segment of involved bowel was resected and the mid-duodenum anastomosed to the proximal ileum. After a stormy course, the patient recovered and has remained well. The author states that the patient, in proper perspective, presented the well known syndrome of scleroderma and Raynaud's phenomenon in all four extremities. In addition, x-ray studies demonstrated the delayed passage of barium in the upper jejunum, as well as the increased caliber of the small bowel and diminution of peristalsis described by Hale and Schatzki as characteristic of scleroderma (Am. J. Roentgenol. **51:** 407, 1944. Abst. in Radiology **43:** 525, 1944).

The second patient was a 35-year-old Negress who complained of abdominal pain, distention, vomiting, diarrhea, and black stools. Free air was demonstrated in the abdomen roentgenographically. At operation no perforation could be found. The proximal jejunum was dilated and the mesenteric lymph nodes were enlarged. No definitive surgery was done. At autopsy, the histologic studies of the small bowel showed fibrosis and collagen infiltration of all elements. No clinical signs of scleroderma were determined.

The third patient was a 23-year old white male with symptoms of acute epigastric distress, weight loss, and nausea. At laparotomy the stomach wall was found thickened and inelastic, as was the proximal duodenum. Similar changes involved the small bowel from the ligament of Treitz distally about 90 cm. The mesentery was thickened and contained lymphatics filled with a peculiar white material leading to the regional lymph nodes, which were soft and enlarged. A biopsy specimen was taken and histologic study showed abundant thick collagen fibers. The authors believe that the appearance of the intestine and the histologic findings were enough to establish the diagnosis of an early stage of collagen disease even in the absence of characteristic roentgen features. In this particular instance the patient had no other manifestations of collagen disease.

Two roentgenograms; 6 photomicrographs; 1 photograph. JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Fluid Levels in the Duodenal Bulb as a Secondary Sign of Adjacent Disease. J. Schaaf and G. Wilhelm. Fortschr. a. d. Geb. d. Röntgenstrahlen **85:** 543–551, November 1956. (In German) (Röntgenabteilung der Medizinischen Universitäts-Poliklinik Heidelberg, Heidelberg, Germany)

Fluid levels in the duodenal bulb are frequently observed and, in the absence of an intrinsic lesion, may suggest the possibility of disease of an adjacent organ. The authors differentiate the following types: (1) sharp fluid level with an air cupola or air-tip formation; (2) poorly defined level with an intermediate level or triple layer formation; (3) level without evidence of air.

Fluid levels were rarely seen in gastritis or duodenitis, in a single case of gastric ulcer, and never in duodenal ulcer. Gallbladder disease appears to be the most frequent cause. Among 2,419 gastrointestinal studies, levels were seen in 319. In 124 of these cases cholecystograms were obtained, showing gallbladder disease in 85. In 43 cases the gallbladder had been removed. Eleven cases had a diagnosis of liver cirrhosis.

Level formations may also be absent in gallbladder disease. For example, a normal bulb was observed in 15 cases of cholelithiasis, and in 8 postcholecystectomy patients. On the other hand, level formations were noted in 36 patients with normal cholecystograms. Nevertheless, the impression prevails that in a high percentage of cases diseases of adjacent organs exist which can produce a fluid level either by extension of peritoneal processes or by viscero-visceral reflexes.

Three roentgenograms; 3 tables.

ERNEST KRAFT, M.D.
Northport, N. Y.

Pneumatosis Cystoides Intestinalis. J. Edwin Alford, Giovanni Galletti, and Gordon J. Culver. Am. J. Surg. **92:** 648–654, November 1956. (Buffalo General Hospital, Buffalo, N. Y.)

The literature is reviewed, with comments upon the various theories explaining the occurrence of pneumatosis of the intestine, notably the mechanical, bacterial, and chemical.

The *mechanical theory* appears to be the most popular. This attributes development of the air cysts to total or partial obstruction of the gastrointestinal tract, with increased pressure forcing small amounts of gas through the intact or ulcerated mucosa. Once the level of the mucosa has been passed by the gas bubbles, they may travel in the mesentery to distant sites along the intestinal tract. Some authors feel that a particularly important concomitant condition is obstruction of the pylorus, usually secondary to peptic ulcer. The *bacterial theory* presupposes penetration of the submucosal and subserosal tissues by gas-producing microorganisms. The *chemical theory* assumes absorption or diffusion of gas bubbles through the mucous membrane of the intestine, as a result of an underlying imbalance or upset of acid-base relationships between the blood stream and intestinal mucosa. Deficient diets and neoplastic cells have also been held responsible.

Two cases are reported. The first patient, a 74-year-old white woman, had constipation alternating with diarrhea with occasional bloody mucus, epigastric distress, anemia, and symptoms suggesting duodenal ulcer. Sigmoidoscopic examination disclosed what appeared to be numerous small sessile adenomas with superficial ulceration and hemorrhage. Biopsies of these lesions, however, were reported as showing normal rectal mucosa. A barium enema study revealed small gas bubbles at the edge of the bowel along the course of the colon from the mid-transverse region to the rectosigmoid junction. An upper gastrointestinal examination disclosed a duodenal ulcer in a deformed bulb. Films six weeks later showed essentially complete resolution of both the colonic air cysts and the duodenal ulcer.

The second patient, a 45-year-old white woman, gave a history of diarrhea and abdominal discomfort for three months. Signoidoscopy, a barium enema study, and an upper gastro-intestinal series revealed no abnormalities. Some small filling defects in the mid-portion of the colon were felt to represent fecal remnants. Similar studies at intervals during the next year led to a diagnosis of pneumatosis cystoides intestinalis, and the patient was admitted for surgery. At operation, the entire colon, excluding only the cecum and rectum, showed multiple, lobulated blebs of grape-like appearance scattered along the course of the colon at the subserosal level. Aspiration yielded air, without bacteria.

The authors feel that the best explanation for their 2 cases is an upset of acid-base relationships in the tissues of the intestinal wall, with diffusion of gases from the intestine followed by gas collection and cyst formation. An important consideration in differential diagnosis appears to be multiple adenomatous polyps.

Six figures; 1 table. JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Pneumatosis Cystoides Intestinalis with Report of a Case. Raymond E. Benson and Grant P. Raitt. Ann. Surg. **144:** 907–912, November 1956. (2722 Third Ave., N., Billings, Mont.)

The authors report a case of pneumatosis cystoides intestinalis in a 9-year-old boy, involving approximately 8 feet of the small intestine. It is thought that intestinal obstruction may have initiated the disturbance. The disease was diagnosed preoperatively by roentgenograms and the patient later recovered spontaneously.

From the roentgenographic standpoint the most remarkable feature was a characteristic double zone of radiolucency separating the dilated intestinal loops. This appearance was interpreted as being due to extraluminal intramural gas cysts between the intestinal serosa and mucosa with the thickened, apposed, serosal surfaces of the adjoining loops producing a linear density bisecting the radiolucent zones. Also noted was free air beneath the diaphragm and retroperitoneal gas shadows outlining the kidneys. A preoperative roentgen diagnosis has been obtained only on rare occasions.

The authors review briefly some of the etiological theories. They believe that, when there is an associated disease state, the proper treatment is to correct the primary condition and leave the pneumatosis alone. In those rare instances where the condition is encountered at laparotomy and no other disturbance of possible etiologic importance can be found, resection may be considered when involvement is limited to a short segment of intestine.

Three roentgenograms; 1 photograph.

Annular Pancreas. Roentgen Manifestations. Maxwell H. Poppel and Samuel L. Beranbaum. Am J. Digest. Dis. **1:** 476–483, November 1956. (Bellevue Hospital Center, New York 16, N. Y.)

Annular pancreas is a congenital anomaly in which

anterior and posterior arms of pancreatic tissue encircle the duodenum either completely or partially with an anterior gap. The abnormal tissue may at times be involved by pancreatitis or carcinoma. Clinically the condition may produce intestinal obstruction at birth or later in life, or symptoms may be minimal or non-existent.

Radiographically, the diagnostic criteria are: (1) duodenal narrowing constant in all films and positions, and unchanged on repeat studies; (2) absence of irritability or tenderness, and no mucosal destruction; (3) small mucosal folds in the narrowed segment; (4) a large, smooth, dilated duodenal bulb (indicating benign obstruction over a long period of time).

Eccentricity of the filling defect suggests duodenal or pancreatic neoplasm. Complete duodenal obstruction in the newborn is more suggestive of atresia, but is not an absolute criterion. Stool examination for occult blood and presence or absence of the stigmata of carcinoma may also assist in the differential diagnosis.

Illustrative radiographs from 16 cases are reproduced, with two brief case histories.

DON E. MATTHIESEN, M.D.
Phoenix, Ariz.

The Use of Radiologic Image Intensification in Chronic Appendicitis. K. Pressler. Fortschr. a. d. Geb. d. Röntgenstrahlen **85**: 551–562, November 1956. (In German) (Hellgrund 141, Wedel/Holstein, Germany)

Fluoroscopic motility studies of the appendix with the image intensifier offer the following advantages over ordinary fluoroscopy: (1) more detail with lower kilovoltage and milliamperage, (2) rapid adaptation of the eyes, although the room need not be completely darkened, (3) less x-ray exposure to the examiner and the patient, (4) more frequent visualization of the appendix (in 91 per cent of cases as compared with 65 per cent in routine examinations).

One hundred patients with suspected appendicitis were examined, but in only 52 of these could the roentgen diagnosis be checked. In 33 cases there was full agreement with the surgical findings (26 cases of appendicitis, 7 normal appendices). In the remaining 19 cases, which came to autopsy, there was disagreement: in 3 apparently normal subjects appendicitis was found pathologically, while in the remaining 16 cases the roentgen diagnosis of appendicitis could not be verified. In 8 of the 48 unverified cases the roentgen diagnosis of appendicitis agreed with the clinical findings. In 35 cases with normal roentgen findings other conditions could be made responsible for the symptoms. In 5 cases, however, the disagreement was unresolved.

Generally speaking, the value of the roentgen signs has remained doubtful, although motility studies have proved to be much more accurate with the image intensifier. The roentgen diagnosis of appendicitis depends upon (1) disturbed motility, (2) localized tenderness, (3) non-visualization of the appendix, and (4) changes in form and fixation. Disturbed motility of the appendix and of the adjacent intestine, with delayed appendiceal filling, have been misleading and can no longer be considered characteristic of appendicitis. Tenderness alone, even together with fixation, is also insufficient for a diagnosis of appendicitis. The more frequent visualization of the appendix with the image intensifier has decreased the errors in diagnosis. The so-called short appendix, especially in retrocecal position and in association with localized tenderness, has proved to be a dependable sign of appendicitis.

Thirty roentgenograms; 5 tables.

ERNEST KRAFT, M.D.
Northport, N. Y.

Roentgen Diagnosis of the Rectum. Lars Andrén and Sture Frieberg. Gastroenterology **31**: 566–570, November 1956. (Allmänna Sjukhuset, Malmö, Sweden)

Contrary to general experience, the roentgenographic visualization of lesions of the rectum may be extremely reliable. The authors attribute their success to thorough bowel cleansing, reduction of mucous secretion, use of a double contrast method in which air is blown into the colon through a small amount of a thick barium mixture in the lower bowel, a long focus-film distance (1.5 meters) to reduce distortion, and meticulous attention to detail.

Previous to the examination the patient is kept on a light diet and purged, preferably with castor oil. Tannic acid is used to reduce secretion. One milligram of atropine is given orally some time before the examination to reduce mucous secretion and to mitigate the pain of bowel contractions. A cleansing agent in the form of Clysodrast (a water-soluble combination of a methane derivative with tannic acid manufactured by AB Ferrosan, Sweden) is added to the cleansing enema. Following this, a thick barium enema mixture, to which Clysodrast is also added, is allowed to run into the colon only as far as the middle of the descending segment. Air is then blown through the mixture, while the patient is rotated, until the bowel is thoroughly distended. A good contrast coating of the entire colon is usually obtained. The surplus barium is drained off so that only the coating on the rectal wall remains. If necessary, additional air is insufflated so that the rectum is sufficiently expanded.

During the last two years almost 3,400 patients have been examined with the technic described. Polyps were found in 343 or 10 per cent of these. In 200 (6 per cent) the polyps were considered to be within rectoscopic level. In 135 of these cases only one polyp was found; in 37 cases there were two polyps, and in 28 three or more. The total number of rectal polyps was 249. Of these, 121 were less than 5 mm. in diameter, measured directly from the x-ray picture without reference to enlargement. Ninety polyps were between 5 and 10 mm. in diameter, and 38 exceeded 10 mm. in size. The authors repeatedly found polyps in the rectum that had been overlooked at rectoscopy. On the other hand, in only 2 cases were polyps detected rectoscopically that were not demonstrable on the roentgenograms.

Seven roentgenograms.

MORTIMER R. CAMIEL, M.D.
Brooklyn, N. Y.

The Roentgenologic Manifestations of Pancreatic Tumors. Frank B. McGlone, Donald S. Robertson, and John M. Grogan. Gastroenterology **31**: 551–562, November 1956. (F. B. M., 1801 Williams St., Denver, Colo.)

The pancreas cannot be visualized directly by roentgen examination. Information about it must be obtained from effects on adjoining structures. The authors reviewed 115 proved pancreatic tumors (4 cysts are included), seen at the University of Colorado School of

Medicine and affiliated hospitals. Ninety-three of the 115 patients had been submitted to roentgen study. Of these, 56 (60.2 per cent) showed some abnormality in contiguous structures.

The tumors were located predominantly in the head of the pancreas (55 cases) or the head and proximal portion of the body (19 cases), producing changes chiefly in the duodenum. In the order of frequency the following roentgen signs were produced (the number of cases appears in parentheses): widening of the duodenal loop (8); lowering of the duodenojejunal angle with obtuse angle (8); ulcer-like defect of the duodenal bulb (6); infiltration of the second portion of the duodenal bulb (6); infiltration of the third portion of the duodenal bulb (6); infiltration of the first portion of the duodenal bulb (5); upward displacement of the duodenal bulb (5); fixation of the duodenum (5); obstruction of the first portion of the duodenum bulb (4); dilatation of the duodenum (4); reverse-three deformity (3); downward displacement of the duodenal bulb (2); evidence of dilated common duct (1).

The stomach was more likely to be involved as the tumor site moved away from the head of the pancreas toward the body. The stomach changes could be classified according to their production by extrinsic pressure or by infiltration. Other organs were occasionally affected as evidenced by the following incidental roentgen findings: jejunocolic fistula (1); choledochoduodenal fistula (1); abnormal cholangiograms (3); pressure defects on the transverse colon (5). The deficiency patterns of the small bowel were observed in 11 cases.

Roentgen defects are absent in a sufficient number of cases that negative findings cannot exclude the presence of a tumor.

Fifteen roentgenograms; 5 tables.

MORTIMER R. CAMIEL, M.D.
Brooklyn, N. Y.

Radiographic Visualization of Multiple Diverticula of the Gall Bladder. Report of Three Cases. Emanuel Friedman and Alan B. Skorneck. New England J. Med. **255:** 940–943, Nov. 15, 1956. (VA Hospital, West Haven, Conn.)

Cholecystographic demonstration of diverticula of the gallbladder (Rokitansky-Aschoff sinuses) is said to have been first reported by March in 1948 (Am. J. Roentgenol. **59:** 197, 1948. Abst. in Radiology **51:** 893, 1948). Since then, 24 additional examples have been recorded. The present authors describe 3 cases of multiple diverticula with localized hypertrophy of the gallbladder wall shown radiographically. Pathological findings in 2 of the cases tend to confirm the thesis that cholecystographic demonstration of such diverticula, particularly in the contraction phase, provide evidence of gallbladder disease.

There are 2 significant roentgen findings: (1) the presence of an apparent stricture in the region of the gallbladder neck, causing the organ to appear double, with the portion proximal to the narrowing more contractile in response to a fatty meal; (2) a rim of bead-like contrast material, seen sometimes before and always after the ingestion of a fatty meal. Even when an apparently well functioning gallbladder is found on radiographic examination, the authors believe that the presence of multiple diverticula calls for surgical intervention.

Two roentgenograms; 1 photograph.

On the Relative Merits of the Oral and Intravenous Methods of Cholegraphy. David Stenhouse. Brit. J. Radiol. **29:** 498–503, September 1956. (Radiodiagnostic Department, Western Infirmary, Glasgow, Scotland)

The author reports examinations of 100 consecutive patients with Biligrafin (Cholografin) given intravenously on one day and Telepaque, administered orally, on the following day, each patient receiving both examinations. The dose of Biligrafin was 20 c.c. of a 20 per cent solution, containing 4 gm. of Biligrafin, and films were made at 10, 20, 60, 90, and 120 minutes routinely. The Telepaque dose consisted of six tablets, with films made at 14 hours and at 10 and 20 minutes after a fatty meal for duct visualization.

Approximately one-half the gallbladders were apparently normal, and in these the shadow was less dense on the two-hour Biligrafin film than on the fourteen-hour Telepaque study. In a few cases, however, in which a five- or six-hour film was made in the Biligrafin study, the shadow was at least as dense as the average Telepaque shadow. Stones were demonstrated in approximately one-fourth of the cases with Telepaque, but in 3 of these were missed with Biligrafin.

No gallbladder shadow was obtained with either method in 20 cases. In 2 cases a shadow was absent with Biligrafin and present with Telepaque; in 1 case the reverse was true.

The bile ducts were visualized in 91 per cent of the series with Biligrafin as compared with 63 per cent with Telepaque. The visualization was denser with Biligrafin and permitted the diagnosis of stones in several instances, where these were not demonstrated with Telepaque.

The author feels that absence of a gallbladder shadow with Biligrafin, provided the ducts are visualized, is fairly reliable evidence of gallbladder disease. He recommends the use of Biligrafin in cases of previous cholecystectomy and in those cases in which demonstration of either the gallbladder or ducts has not been obtained with Telepaque.

Eight roentgenograms; 1 table.

DAMON D. BLAKE, M.D.
Bowman Gray School of Medicine

New Cholecystographic Technic. Franco Pirastu and Vincenzo Racugno. Radiol. med. **42:** 1085–1088, November 1956. (In Italian) (Istituto di Radiologia Medica dell'Università di Cagliari, Cagliari, Italy)

According to the medical literature, aside from oral administration, cholecystographic media have been introduced into the body intravenously, through the rectum, into the sternal bone marrow, and even directly into the gallbladder, percutaneously, during peritoneoscopy, or through a catheter. The authors have studied the absorption of iodinated organic compounds injected into the peritoneal cavity, and found that granular suspensions and colloids penetrate the lymphatic channels, while crystalloids and water-soluble substances can enter the capillary system. In their experience, intraperitoneal injection of 20 c.c. Biligrafin was followed by good concentration of the contrast material by the gallbladder within about one hour, with optimum visualization at two hours. The procedure is recommended only for those cases in which the oral and intravenous routes are impracticable.

Three roentgenograms.

E. R. N. GRIGG, M.D.
Cook County Hospital, Chicago

Cholecystangiography Using Biligrafin Forte. F. G. Anderson. Brit. J. Radiol. **29:** 504–507, September 1956. (Walton Hospital, Liverpool, England)

The author reports a series of 33 examinations on 31 patients, employing Biligrafin Forte. This drug has the same chemical composition as Biligrafin I.V., but is made up as a 50 per cent solution containing 10 gm. of the active substance, which represents nearly twice the iodine content of the original medium. All of the patients were adults, and 24 were known to have an intact biliary tree; 15 had been examined by the usual oral method, with Telepaque, without visualization. Seven of the patients had had a cholecystectomy some time in the past. The study was carried out after twelve hours of fasting but without other preparation. A scout film was obtained and 20 c.c. of Biligrafin Forte was then injected intravenously in three to four minutes, following which four films were taken at fifteen-minute intervals and a further film at two and one-half hours. A fatty meal was then administered and a film taken thirty minutes later.

One patient had a severe reaction, with peripheral circulatory failure ensuing three to four minutes after completion of the injection, but recovered after the administration of adrenalin. Two failures of visualization were encountered, one in a deeply jaundiced patient and another in a patient with cirrhosis. Visualization was poor in a patient shortly after recovery from infectious hepatitis.

Forty cubic centimeters of Biligrafin Forte was administered on four occasions without further improvement in visualization.

Nine roentgenograms; 1 table.

JOSEPH E. WHITLEY, M.D.
Bowman Gray School of Medicine

Cholografin Methylglucamine. New Contrast Medium for Intravenous Cholangiography and Cholecystography. William H. Shehadi and Issa Sabbag. Am. J. Digest. Dis. **1:** 466–475, November 1956. (New York Polyclinic Medical School and Hospital, New York, N. Y.)

Cholografin Methylglucamine (methylglucamine iodipamide) is an improved medium developed to supersede Cholografin (sodium iodipamide) for intravenous cholangiography and cholecystography. Chemically the new medium is quite similar to Cholografin, and general indications and contraindications for its use are the same.

Cholografin Methylglucamine is a superior agent, however, in that it produces fewer side reactions, is more easily administered, due to the smaller volume of required dose, and in early studies has often given a better outline of the biliary tract.

This superiority was revealed in 100 examinations which the authors carried out as an initial study. The excretion pattern of the medium was found to be practically identical with that of Cholografin; and the best results were obtained by making films at ten-minute intervals up to sixty minutes.

The authors have made the incidental observation that routine administration of a meal of simple fats the evening before examination increases the incidence of gallbladder visualization, evidently by producing a preliminary biliary drainage.

Six roentgenograms; 3 tables.

DON E. MATTHIESEN, M.D.
Phoenix, Ariz.

Intra-Abdominal Fistulae. G. S. Sarin. Indian J. Radiol. **10:** 214–220, November 1956. (Irwin Hospital, New Delhi, India)

Roentgenology plays a dominant role in the recognition of intra-abdominal fistulas and their detailed investigation, without which surgical approach would be difficult. The fistulas are usually secondary to either an inflammatory or neoplastic ulceration, or the result of perforation by a stone. Rarely, they may be postoperative.

Eight cases are presented: 2 of cholecystoduodenal fistula; 2 of choledochoduodenal fistula; 1 of a dermoid cyst in the anterior abdominal wall communicating with the small intestine, with an external fecal fistula following incision by a quack; 1 of subphrenic and perihepatic abscess draining into the colon; 1 of postoperative perforation of the sigmoid colon; 1 of duodenocolic fistula presumably incident to an inflammatory process in the colon.

Eleven roentgenograms.

HERNIA

So-Called Traumatic Diaphragmatic Hernia. A. Brunner. Schweiz. med. Wchnschr. **86:** 1329–1335, Nov. 24, 1956. (In German) (Chirurgische Universitätsklinik Zurich, Zurich, Switzerland)

Non-penetrating injuries of the trunk may cause a strong increase in pressure in the abdomen, leading to rupture of the diaphragm. Since, under such circumstances the serous membranes are also torn, the subsequent prolapse of the abdominal organs into the chest is almost always a *false hernia*. The suddenly occurring wide communication between the thoracic and abdominal spaces, with inevitable changes in pressure, would be expected to result in severe functional disturbances, yet it is often completely asymptomatic.

Ten cases are reported, in 9 of which the rupture involved the left side of the diaphragm, apparently because the liver acts as a protective cushion on the right. The tear may, however, be in the right diaphragm, and an appropriate example is included. One case in this series was the result of a shoulder injury, and it is to be expected that obscure casualties will be present with the mounting rate of traffic accidents.

Roentgenologic proof of prolapse of abdominal organs into the chest is to be considered *per se* an indication for surgical intervention, since absence of symptoms is never a guarantee against future bowel obstruction.

Seventeen roentgenograms.

E. R. N. GRIGG, M.D.
Cook County Hospital, Chicago

THE MUSCULOSKELETAL SYSTEM

Study of Development of Primary Chronic Polyarthritis. M. Hunziker and J. M. Bivetti. Schweiz. med. Wchnschr. **86:** 1275–1279, Nov. 10, 1956. (In German) (Röntgeninstitut der Universität Zurich, Zurich, Switzerland)

This paper is based on the clinical records of 100 patients of the Rheumatology Clinic of the University of Zurich, classified as having primary chronic polyarthritis (rheumatoid arthritis). The earliest complaints were non-characteristic joint pains in the fingers (in rare cases, the disease may start out as a peritendinitis), followed by visible swelling of the proximal interphalangeal articulations of index and middlefinger, extending

later to other digits. In advanced stages, the skin over the metacarpo-phalangeal joints is reddened and tender (inflammatory changes). Typical signs, such as ulnar deviation of the second through the fifth fingers and subcutaneous nodules, especially along the proximal portion of the ulnar margin, appear only in late phases. Involvement of the joints elsewhere in the body is not pathogonomonic, except perhaps for the oft encountered symmetry.

Typical laboratory findings include a high sedimentation rate, a positive agglutination test for hemolytic streptococci (the assumed etiologic allergen), a spiking titer of antistreptolysin, an increase in serum copper, a decrease in serum iron, and, in the long run, a hypochromic anemia. The median age of onset in the series reported (31 males and 69 females) was forty-six years, though most textbooks give it as between twenty and forty years.

A total of 532 roentgenograms, accumulated from these 100 patients, included 238 of the hands, 126 of the feet, 52 of the elbows, 40 of the shoulders, and 46 of the knees. Minimal degrees of *band-shaped periarticular osteoporosis* can be recognized only by comparison with roentgenograms from unaffected individuals. Diffuse osteoporosis, due to atrophy of disuse and systemic factors, is a late feature. Orthograde projections are necessary to identify the seldom encountered widening of the interphalangeal articulations (effusion); *narrowed joint spaces* become more frequent as the disease progresses. Foci of subchondral osteolysis result in *cysts of the spongiosa*, which must not be confused with pseudocysts found in healthy persons in both the heads and bases of phalanges. The cortex over the cyst may be subsequently reabsorbed, and further bone destruction can occur, leading to *punched-out* areas, which have a characteristic appearance. *Periosteal reaction* is seen in the shafts of the metatarsals, metacarpals, and proximal phalanges, rarely adjacent to the distal extremities of radius and ulna. *Deviations*, which are always toward the ulnar side, start invariably with the fifth digit; *subluxations* complete the characteristic appearance, which resembles a tree forced by the wind to crooked growth. *Ankylosis* is the final, "healed" stage, and may be fibrous (joint space preserved on roentgenograms) or osseous (bone trabeculation bridging over the articular surfaces). Differentiation between these two types is of importance for treatment (physical therapy may improve a poor position caused by fibrous, but not one due to osseous, ankylosis). This may require body-section roentgenography.

Band-shaped periarticular osteoporosis is the earliest change to appear, but in the feet this cannot be distinguished from generalized osteoporosis. In fact, because of anatomical considerations, cysts of the spongiosa and narrowed joint spaces are of less importance in the feet than punched-out areas. Careful scrutiny is necessary in all early cases, because periarticular rarefaction, and especially shallow punched-out areas may be overlooked. On the other hand there is always a latent period, sometimes prolonged, so that roentgen findings may be absent for two or three years after the appearance of clinical symptoms.

Treatment is discussed at some length. Physical therapy is strongly recommended, and mobilization of the affected joints is necessary to prevent ankylosis in other than functional position. Balneotherapy is considered in the late stages. The prognosis is fairly good in early cases, in 80 per cent of which some improvement may be obtained. As soon as osseous lesions have appeared, the outlook becomes darker and, although it may take one or two decades, increasing invalidism will supervene.

Six roentgenograms; 5 tables; 5 graphs.

E. R. N. GRIGG, M.D.
Cook County Hospital, Chicago

Disorders of Osseous Structure and Destructive Lesions in the Course of Ankylosing Spondylarthritis. F. Jacqueline. J. de radiol. et d'électrol. **37:** 887–893, November-December 1956. (In French) (Aix-les-Bains, France)

Ankylosing spondylarthritis affects the spine and the sacroiliac and hip joints. When the process is apparently stable, destructive changes may appear in certain areas in the spine and hips. Joint height is maintained and fusion of joints progresses in an orderly manner. Trauma, such as may occur in a fall or during surgery, may accelerate the destructive changes at various levels. In these patients the evolution is different, the changes are more pronounced, and disability may be increased.

Seven roentgenograms.

CHARLES M. NICE, JR., M.D., Ph.D.
University of Minnesota

Correlation of Pain and the Roentgenographic Findings of Spondylosis of the Cervical and Lumbar Spine. Allen E. Hussar and Emanuel J. Guller. Am. J. M. Sc. **232:** 518–527, November 1956. (Veterans Administration Hospital, Montrose, N. Y.)

The authors differentiate between spondylosis and degenerative joint disease, called also osteoarthritis, hypertrophic arthritis, and degenerative arthritis. The term spondylosis they use to denote "the roentgenographic findings of bony spurs of the vertebral bodies, narrowed disc space and narrowed intervertebral foramina occurring singly or in various combinations." The term degenerative joint disease, or osteoarthritis, is reserved for the degenerative changes in the only true joints of the spine, namely, the costovertebral and the apophyseal joints (the articular facets).

The investigation described in this paper was undertaken with the thought that sampling the general population might provide better controlled material for re-examination of the clinical significance of spondylosis. It is based on examination of 500 male employees of the Veterans Administration Hospital at Montrose, N. Y., ranging in age from eighteen to sixty-five years with an average of thirty-six years. Films of the cervical and lumbar spine were taken in the anteroposterior, lateral, and two oblique projections. The films were examined for the presence of bony spurs, narrowing of disk spaces, narrowing of the intervertebral foramina, and abnormality of the apophyseal joint. Those with other deviations from normal were eliminated from the investigation. The following conclusions were reached:

"1. As a rule, pain is not associated with the roentgenographic findings of bone spurs, narrowed disc space or intervertebral foramina of the cervical and lumbar spine.

"2. It is conceivable that pain may be produced by the encroachment of a bone spur, protrusion of a disc or narrowing of a foramen, upon a by-passing nerve trunk, thus producing the symptoms of radicular compression. This occurrence, however, is probably more an excep-

tion rather than a natural sequel of spondylosis. Routine roentgenograms are of dubious value in the diagnosis of encroachment on the nerves by spondylotic changes.

"3. It is suggested that the common practice of labeling a patient with the diagnosis of "degenerative joint disease" (or "osteoarthritis," "hypertrophic arthritis") of the spine because of roentgenographic findings of spondylotic changes should be abandoned."

Eight diagrams; 10 tables.

ALFRED O. MILLER, M.D.
Louisville, Ky.

Bone Changes in Hemiplegia of Early Onset. F. E. Dreifuss. Brit. J. Radiol. **29:** 601–604, November 1956. (National Hospital, Queen Sq., London, W. C. 1, England)

The clinical material reviewed in this paper consisted of 50 patients with hemiplegia of "early" onset. The age range was from four to fifty years and the duration of the hemiplegia from three to fifty years. Tabulation was made of skeletal changes, including skull asymmetry, thickening of the calvarium, ipsolateral frontal and ethmoid sinus enlargement, reduced size of the ipsolateral middle fossa, reduction in length and/or cortical thickness of tubular bones, and epiphyseal dysgenesis. An effort was made to correlate the skeletal findings with the sensory and motor function.

The data indicate that skull and/or extremity changes were present in one form or another in most patients. The upper limbs were almost invariably more severely affected than the lower.

The only correlation obtained was that, in general, agenesis paralleled loss of power. The age of onset of the hemiplegia did not appear to be relevant so long as it occurred before puberty. The maximum growth lag seemed to be in the early years following the onset of hemiplegia, the relative disproportion remaining fairly static thereafter. It is concluded that the agenesis can be accounted for on the basis of disuse during the period of growth.

G. M. STEVENS, M. D.
Palo Alto, Calif.

Hyperparathyroidism and Steatorrhoea. D. R. Davies, C. E. Dent, and A. Willcox. Brit. M. J. **2:** 1133–1137, Nov. 17, 1956. (University College Hospital and Middlesex Hospital, London, England)

Two cases of steatorrhea are described in which roentgen signs thought to be specific for hyperparathyroidism were found. In both cases osteosclerosis of the vertebral bodies was demonstrated, such as may sometimes be found in renal disease. In one case the serum calcium level was consistently 9–10 mg. per 100 ml. In this instance, treatment with vitamin D led to a remission of the bone pains and of the radiological signs of osteomalacia and hyperparathyroidism. In the second case the plasma calcium level was 11–12 mg. per 100 ml. Some relief of bone pains followed treatment with vitamin D, and the calcium balance responded in the expected way. There was, however, no change in the x-ray signs of hyperparathyroidism. Symptoms were relieved and plasma calcium and roentgen signs returned toward normal temporarily after one, and permanently after a second, parathyroid adenoma had been removed.

The authors interpret their findings to mean that hyperparathyroidism may sometimes occur in steatorrhea. It can at first be reversed by giving vitamin D. It may, however, become uncontrollable by this means, in which event it produces a clinical picture easily confused with primary hyperparathyroidism. When this happens, hyperparathyroid bone changes are combined with those of osteomalacia, and the urine calcium level is low (not high, as in primary hyperparathyroidism). Page (Arch. Middlesex Hosp. **4:** 215–218, July 1954) has described a case of parathyroid adenoma associated with pancreatic steatorrhea. It would appear that roentgen signs of both osteomalacia (or rickets) and hyperparathyroidism can occur in steatorrhea as well as in renal osteodystrophy.

Eleven roentgenograms; 1 photograph; 3 graphs.

GYNECOLOGY AND OBSTETRICS

Hysterosalpingography in the Treatment of Infertility. Roy A. Walther, Jr. Missouri Med. **53:** 956–960, November 1956. (Missouri Baptist Hospital, St. Louis, Mo.)

Of a series of 24 patients undergoing hysterosalpingography, 15 became pregnant within six months, a pregnancy rate of 62.5 per cent. Two became pregnant twice, each time following hysterosalpingography, which raises the incidence to 65.4 per cent.

The author describes this procedure as a simple and painless one, requiring little special equipment. No routine preoperative medication is necessary. Only 1 patient (suffering from endometriosis) complained of abdominal discomfort. A water-soluble medium, Salpix, was used in the present series, and small amounts were found to produce excellent radiopacity, with no untoward effects. A twenty-four film is neither necessary nor advisable.

Four roentgenograms; 1 table.

THE GENITOURINARY SYSTEM

Size of Normal Kidneys. Hans Moëll. Acta radiol. **46:** 640–645, November 1956. (University Hospital of Lund, Lund, Sweden)

Anatomically, the left kidney is slightly larger than the right, and the kidneys of men are slightly larger than those of women. Roentgenographically, the differences have not seemed so clearly apparent.

The author, after a meticulous roentgen study of the kidneys in a group of 50 clinic patients (with no evidence of renal disease) and 115 healthy soldiers, makes the following observations:

1. Kidney size and contour correspond to total body surface and habitus.
2. The kidneys are slightly smaller in women than in men.
3. The left kidney is somewhat larger than the right in both sexes.
4. Kidney size does not change in the fasting state.
5. Average sizes are: For men: right, 12.7 × 6.3 cm.; left, 13.2 × 6.4 cm. For women: right, 12.4 × 5.9 cm.; left, 12.8 × 6.1 cm.

Three tables.

DON E. MATTHIESEN, M.D.
Phoenix, Ariz.

THE ADRENALS

Radiological Diagnosis of Diseases of Adrenal Origin. John G. McAfee and Carl E. Balli. Am. J. M. Sc. **232:** 572–599, November 1956. (Johns Hopkins University and Hospital, Baltimore, Md.)

This is a 25-page review dealing with the classification and principal characteristics of diseases of adrenal ori-

gin and the various radiological methods for their investigation. The bibliography includes 206 references.

Diagnostic methods discussed include plain roentgenography of the abdomen, intravenous pyelography, presacral gas insufflation, abdominal aortography and laminagraphy, which may be used successfully with some of the other technics.

Gas embolism, and other complications of gas insufflation are well covered. One recent report of 58 deaths due to gas embolism collected in response to a questionnaire addressed to members of the American Board of Urology included 34 from perirenal injections and 24 from presacral injections. In addition, there were 64 severe, non-fatal reactions, of which 31 occurred as a result of perirenal injections and 33 following presacral injections. All these deaths occurred with air, oxygen, or helium, but none occurred with the use of carbon dioxide or nitrous oxide, because of their high solubility in blood (Ransom: J. Urol. **76**: 664, 1956).

This fine and comprehensive article should be read in its original form.

Twelve roentgenograms; 1 table.

ALFRED O. MILLER, M.D.
Louisville, Ky.

TECHNIC

Development of Apparatus and Methods for Roentgen Studies in Haemodynamics. Åke Gidlund. Acta radiol. (suppl. 130) pp. 1–70, 1956. (St. Eriks Hospital, Stockholm, Sweden)

In this monograph the author describes two film changers which he has developed for direct roentgen cinematography. Both can be used for single-plane work or be coupled in two-plane devices for simultaneous radiography. Rates of exposure with these apparatuses vary from one every two seconds to eighteen per second.

The injection of contrast medium for angiocardiography is achieved by use of a high-pressure motor-driven injection syringe also developed by the author. By regulation of the pressure, varying velocities of injection are achieved for different catheters. The apparatus maintains the temperature of the medium at 37° C. Remote control is provided to reduce exposure to operating personnel. To inject peripheral vessels the lower-pressure injector is used without a heating system. In this apparatus the piston is stationary while the cylinder moves to fill and empty the syringe

Experiments were carried out with various cannulas and catheters to test their efficiency. Tapering the distal ends of cannulas was found to reduce interference with flow in the punctured vessel. Movement of a catheter backward within a vessel as a result of pressure by the injected medium is eliminated by closing the tip of the catheter and letting the fluid escape in a lateral direction. In thoracic aortography, to achieve contrast filling of the aortic arch but not of the coronary vessels, a catheter with a mouthpiece in its side walls and closed at the tip was found most efficient. Experiments showed that with such a catheter with a perforated mouth-piece, injection speed could be five times as great, without contrast filling of the coronary vessels, as when the injection was made through a cannula.

Studies were carried out to determine the flow characteristics of blood and other fluids. The kinematic viscosity of Umbradil 40 per cent and 70 per cent used in roentgenography of the vessels was found to be lower than that of blood, but was adjusted to blood level by the addition of polyvinyl pyrrolidone (PVP).

Pressure determinations were made in circulation models constructed to simulate the heart and vessels. When water was injected at a rate of 25 c.c. per second through a catheter into an "aorta" whose cross-section was 100 times that of the catheter, no change in pressure due to the injection or the presence of the catheter could be demonstrated. Nor was any pressure effect discovered in smaller vessels the ratio of whose cross-section to that of the catheter exceeded 50 : 1 when the velocity of flow was less than 10 c.c./sec.

Studies were also made in patients following catheter injection into the distal aorta and femoral arteries. Satisfactory serial films showing the progression of the contrast medium were obtained by making exposures of 0.12 second at intervals of 1 second. A sharp boundary at the advancing margin of the contrast medium was seen only in the slower phases of pulsatile flow and slow stationary (even) flow.

The velocity of flow in the femoral arteries was measured in several patients. Photomultiplier tubes placed above the vessels detected differences in the density of the contrast medium (injected at a constant rate) related to the rate of flow in the vessels. By recording the impulses received from two such photomultiplier tubes over the femoral arteries and relating them to a time axis, the velocity of flow in the arteries was determined. The pulses were measurably diminished when a blood-pressure cuff placed immediately distally was inflated, and the author postulates that a similar phenomenon would occur in front of an area of stenosis in a vessel. Readings were obtained in one patient with stenosis in a distal part of the femoral artery (verified by arteriography) which showed the appearance of a stationary (*i.e.*, even) flow rather than the normal pulsatile characteristics.

Fifty-nine figures.

ARTHUR S. TUCKER, M.D.
Western Reserve University

A Simple Apparatus for Rapid Serial Roentgenography: Design, Construction, and Operation. Peter P. Poulos, James S. McGoey, and Laurence Miscall. Arch. Surg. **73**: 839–843, November 1956. (L. M., Triboro Hospital for Thoracic Disease, Jamaica, N. Y.)

Experience has shown that angiocardiographic studies are most informative when multiple serial roentgenograms are made at very short intervals during the passage of the contrast medium through the heart and great vessels. Although cineroentgenography ultimately may become the method of choice in such examinations, at present not only is its detail inferior to that of direct roentgenography but the equipment is expensive and its use rather technical. The trend has been toward rapid serial exposures with the use of either roll film or lightweight cassettes.

This report details the construction of a simple, efficient safe cassette changer which permits exposures of serial films (11 × 14 inches), at a more rapid rate than one per second.

Three figures; 1 table.

Exposure Factor Selection by Means of a New Calculator. M. Simon. Brit. J. Radiol. **29**: 588–595, November 1956. (Diagnostic X-ray Department, Guy's Hospital, London, S.E. 1, England)

The author describes the theory, derivation of scales,

and application of a system for the selection of each of the variable exposure factors for obtaining a radiograph of desired density. This system has been put into compact and usable form as a circular calculator made up of two series of interlocking disks. One set of disks indicates the correct exposure for any part, based essentially on the patient's weight, when the average exposure factors are known for a certain part and modification for individual variation from the normal is needed.

The second set of disks, on the opposite side of the device, provide for modification of exposure factors by determination of the thickness of the part being filmed and consideration of a density correction factor. The latter allows for the effect of filters, cones, grids, type of film used, screens, etc., by assessing their effect on film density as compared with the alteration of density produced by 1 cm. of average human soft tissue at 70 kv.

The author indicates that the calculator may become available in prepared form if interest warrants. This paper does not lend itself to summary. Interested persons should read it in its original form. Diagrams, charts, and representative films taken with the calculator's aid are incorporated in the text.

Twenty-four roentgenograms; 9 drawings.

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Palo Alto, Calif.

Medical Aspects of the Image Intensifier. J. Feddema. Indian J. Radiol. **10**: 237–242, November 1956.

Tests carried out on a "Philite" phantom, as designed by Burger, for a subject thickness corresponding to that of the human thorax have shown that, at the same x-ray tube voltage, fluoroscopy with the image intensifier produces roughly the same contrast-detail perceptibility at 0.1 ma. as ordinary fluoroscopy at 4 ma. The actual contrasts are the same with as without the intensifier, but with it they are raised to a higher luminescence level.

In photography with the image intensifier, the image quality is limited not only by the blurring effect of the two fluorescent screens, but also by the grain of the film. It has been found that the x-ray intensity required to take an image intensifier photograph on Kodak "Micro-File" film, with a tandem optical system, each component having an aperture ratio of 1 : 1.5, is only from a half to a quarter of that involved in the taking of an ordinary full-size roentgenogram of the same subject at the same tube voltage.

While a disadvantage of image intensifier photography compared with ordinary screen photography is the small viewing field, this may be offset by several advantages: the apparatus is relatively small and easy to handle; adjustments prior to taking photographs are readily effected without preliminary dark-adaptation; single photographs can be taken on fine-grain 35-mm. film giving high contrast and therefore excellent picture-quality; and all these advantages are procured with an x-ray dose smaller by at least a factor of 3 than that required in ordinary roentgenography.

To all appearances, cinematography with the image intensifier is the only method of photographing transient processes in the human body without risk either to the subject (overdose) or to the x-ray tube (overloading). Experience has shown that the dose needed to expose a single photograph on a more sensitive 35-mm. film is less than one-tenth of the dose ordinarily employed in roentgenography.

A general survey of the use of the image intensifier in skeletal, spinal, otorhinolaryngological, digestive, genitourinary, pulmonary, and heart examinations is given.

Two roentgenograms; 1 photograph; 2 tables.

A Preliminary Report on the Use of Cesium Chloride in Contrast Radiography. Robert Shapiro. Acta radiol. **46**: 635–639, November 1956. (Yale University School of Medicine, New Haven, Conn.)

The preliminary trial use of cesium compounds for contrast radiography is reported upon in this article. Cesium chloride appears to have the lowest toxicity of the various cesium salts, and a 30 per cent solution produces satisfactory radiopacity.

When bronchography was performed with this material it was necessary to add thickening agents to the solutions to prevent too much alveolar filling and too rapid absorption from the bronchopulmonary tree. Trial use of the solutions in man produced severe chest pain and caused hyperemia and epithelial injury which was later surgically verified.

Use of the material for hysterosalpingograms on dogs seemed satisfactory, and had no evident toxic effect.

Three roentgenograms; 1 table.

DON E. MATTHIESEN, M.D.
Phoenix, Ariz.

RADIOTHERAPY

The Influence of Histological Structure on the Radiosensitivity of Tumours: A Symposium. I. The Histological Aspects of Tumour Radiosensitivity. R. W. Scarff and P. S. Andrews. Brit. J. Radiol. **29**: 478–482, September 1956. (Bland-Sutton Institute of Pathology, Middlesex Hospital, London, W. 1, England)

II. The Influence of Systemic Factors on the Differentiation and Radiocurability of Cervical Cancers. A. Glucksmann. Brit. J. Radiol. **29**: 483–487, September 1956. (Strangeways Research Laboratory, Cambridge, England)

III. The Role of Histology in the Treatment of Breast Cancer. H. J. G. Bloom. Brit. J. Radiol. **29**: 488–497, September 1956. (Meyerstein Institute of Radiotherapy, Middlesex Hospital, London, W. 1, England)

Opening this Symposium on the radiosensitivity of tumors as influenced by histology, Scarff and Andrews cite Warren's classification (Am. J. Roentgenol. **45**: 641, 1941). Not only do the dividing, resting, and differentiating cells of which the tumor is made up have different radiosensitivities, but other factors are recognizable histologically, bearing on the stroma. The authors consider stromal reaction, diet, fibrosis, previous irradiation, acquired radioresistance, and anaerobiosis. Under each of these headings the literature, including both animal and human experiments, is briefly surveyed. Photomicrographs are included demonstrating the pre- and post-irradiation appearance of four tumors, illustrating that in an individual case the degree of differentiation does not determine the radiosensitivity. It is pointed out that sampling errors may become large if only a small fragment of tissue is obtained to be studied histologically.

Glucksmann states that the histological structure as

well as the local radiocurability of a tumor depends on systemic factors. This is suggested as one of the reasons why the response to radiation therapy of a given tumor cannot be predicted from the histologic appearance prior to treatment. On the other hand, a positive correlation between the degree of maturity of squamous-cell cancers and local curability can be established statistically for different sites.

The five-year survival rates for 898 cervical cancers receiving intracavitary radium therapy, and classified both as to the stage of disease and differentiation, are presented, showing a significantly higher survival rate for the differentiated as compared with the anaplastic types.

It is not the mere presence of differentiation before treatment, however, which is the decisive factor, but the functional capacity of the tumor to respond to irradiation with increases in the extent and degree of differentiation. This capacity can be assessed only by serial biopsies before and during treatment.

In squamous-cell cancer keratinization is evidence of differentiation. Inhibition of mitosis, degeneration of dividing cells, and sloughing of tumor masses due to vascular and inflammatory changes are other effects of radiation observed even in lesions which prove not to be radiocurable. In adenocarcinoma, mucification is induced by irradiation in radiocurable growths and is another example of differentiation promoted by radiotherapy in suitable tumors.

To illustrate the relation of differentiation and local curability of tumors to systemic factors, Glucksmann uses a series of mixed carcinomas of the cervix, varying in maturity from types with separate strands of squamous and columnar components to types incapable of full differentiation. These tumors show a high degree of association with pregnancy; also the five-year survival rates are disappointingly low. The association of special histologic types of tumor with pregnancy suggests that the concomitant hormonal changes may contribute not only to the causation of cancer but may also play a role in determining the type. This leads the author to speculations on the efficacy of coupling hormonal treatment with radiotherapy as well as on the mechanisms of tumor response. He concludes with a plea for a better understanding of the processes of differentiation and the factors influencing this process to help render tumors curable which are so far refractory to therapy.

Twelve photomicrographs are reproduced.

In the final contribution, Bloom seeks to apply histologic studies to the problem of radiocurability of mammary cancer. A series of 1,002 carcinomas of the breast were graded histologically and staged clinically. Histologic grading was found to provide a useful guide to prognosis. Taken alone, however, it appears to be no more useful in classifying cases than a clinical staging system. Results with the two methods are in general comparable. By combining stage and grade, a classification can be obtained which takes into account not only the apparent extent of the tumor but also its potential malignancy. This probably provides the most accurate guide to prognosis available at the present time and may assist in the search for the most suitable treatment for individual patients according to the nature and extent of the growth.

Seventeen photomicrographs and 10 photographs illustrate this paper.

JOSEPH E. WHITLEY, M.D.
Bowman Gray School of Medicine

The Technique of Treating the Pituitary Gland with Roentgen According to the Pendulum Principle. Bengt H. O. Rosengren. Acta radiol. **46**: 668–675, November 1956. (University of Gothenburg, Gothenburg, Sweden)

In order to deliver 5,000 r to the pituitary area by conventional x-ray irradiation a dose of about 3,600 r to each of four skin fields is required, leading to such unfavorable reactions as dry epidermitis and more or less permanent pigmentation, epilation, and possibly subsequent telangiectasis and atrophy of the skin. Rotational and pendulum irradiation technics make it possible to eliminate such reactions by spreading the skin dose over a larger area. If required, considerably greater doses can then be given without any risk of an overdose.

Pendulum therapy is so directed as to spare the hairy parts of the head. Two different planes may be used. In one the treatment zone covers a band extending from the pituitary point of projection of one temporal area to that on the opposite side, passing over the center of the forehead. The second is defined by the two temporal points and the tip of the nose.

Because the areas in front of and below the hypophysis are largely air-containing, while above and behind is the homogeneous brain substance, secondary irradiation from the two areas is not uniform. In addition, the air-containing sinuses cause increased transmission. Measurements with phantom and ionization chamber showed the dose to the pituitary to be 35 per cent greater when the plane through the tip of the nose was used than with the plane through the forehead. With either plane the treatment ray should be centered directly on the pituitary, and lead eye-protectors are necessary.

Seven diagrams.

DON E. MATTHIESEN, M.D.
Phoenix, Ariz.

Radiotherapy and Intra-Ocular Metastases. Ed. Rosselet and P. J. Rosselet. Radiol. clin. **25**: 355–358, November 1956. (In French) (Université de Lausanne, Lausanne, Switzerland)

Seventy-five per cent of ocular metastases have their origin in cancer of the breast. Tumors from the alimentary canal and the bronchus are responsible for only 10 per cent. One cancer of the breast in 200 metastasizes to the choroid and this metastasis may be the only one clinically evident. The prognosis for vision depends heavily on how early the diagnosis is made and treatment is instituted, as well as on the radiosensibility of the tumor.

A choroid metastasis usually displaces the retina, but does not tear it, and produces impairment of vision and changes in the visual field. The apparently healthy eye should be carefully examined because in one-fifth of the cases the involvement is bilateral.

The authors present the history of a 51-year-old woman who had a carcinoma of the breast treated surgically and with irradiation two years before the appearance of the metastasis. Two courses of therapy were given to one eye, and one course to the other eye, over a period of three years, with excellent results in restoration of vision before widespread metastases resulted in death. It is interesting to note that the lens of the right eye received 9,000 r and that of the left 9,750 r, with no loss in transparency.

CHRISTIAN V. CIMMINO, M.D.
Fredericksburg, Va.

The Management of Lingual Cancer. Frank E. Berridge, Jr., and Arthur G. James. Surg., Gynec. & Obst. **103:** 595–606, November 1956. (University Hospital, Ohio State University Medical Center, Columbus, Ohio)

This is primarily a surgical paper. The authors discuss the occurrence, history, clinical features, pathology, and diagnosis of cancer of the tongue in the light of experience gleaned from 102 consecutive cases of primary lingual cancer in patients admitted to the head and neck service of the Ohio State University Hospital in 1948 through 1955. They discuss the surgical treatment of this disease, from partial glossectomy, through hemiglossectomy and radical neck dissection, to what they term the "commando" operation. Included also is a general discussion of the type of anesthesia and postoperative maintenance. In a fair percentage of their series of patients they have combined surgery with interstitial implantation of radioactive iridium loaded into hollow nylon threads at 1 cm. intervals. A tumor dose of 6,000 r is delivered whenever possible. Externally applied deep roentgen therapy is used to supplement the interstitial source when the need exists.

The indications for radiation therapy in lingual cancer are given as follows: cases considered inoperable with bilateral cervical or distant metastases or extension to the base of the skull, lymphomas of the lingual tonsil or the base of the tongue, local recurrences following a radical neck dissection, or residual cancer tissue after radical surgical resection.

The authors state that the advent of the radical neck dissection by Crile in 1906, coupled with modern methods of asepsis, anesthesia, blood replacement and antibiotics, has restored the surgical treatment of lingual cancer to its former eminence. The overall operative mortality in their series of 102 patients was 2.5 per cent. No figures are given as to results of treatment.

Two roentgenograms; 8 drawings; 1 table.

JAMES E. BAUER, M.D.
University of Missouri

Carcinoma of Larynx. Results of Roentgen Therapy During a Period of Fifteen Years (1937–1952). Edward L. Jenkinson, Lillian Kao, Paul H. Holinger, K. C. Johnston, and R. W. Donnelly. Am. J. Roentgenol. **76:** 942–948, November 1956. (E. L. J., 1439 S. Michigan Ave., Chicago 5, Ill.)

The authors here analyze a series of 109 unselected cases of carcinoma of the larynx treated with external irradiation. All were histologically verified and were followed for varying periods from three to ten or more years. Sixty-eight patients were in a far advanced stage of disease, 45 of these with metastatic cervical lymph nodes. Twenty-seven of the patients had had previous treatment elsewhere; 4 roentgen therapy and 23 surgery. Sixteen of the latter group had had total laryngectomy.

An overall cure rate of 34 per cent (based on 89 "determinate cases") was attained in this entirely unselected group of patients. Cure rates ranged from a high of 78 per cent for Stage I to 18 per cent for Stage IV, serving to emphasize the importance of early diagnosis. Intrinsic lesions (those involving the true cords, false cords, laryngeal ventricle, and anterior commissure) were cured three times as often as those in the extrinsic group (61 per cent and 21 per cent respectively). The authors feel that this difference is referable at least in part to the fact that intrinsic lesions are generally found in an earlier stage, while extrinsic tumors tend to be advanced when first seen. From the radiological standpoint, the size and extent of the lesion when treatment is undertaken are thought to be more important factors in evaluating prognosis than the site of the tumor *per se*. In this series the best survival rates are seen with the true cord lesions, particularly those with free motility of the cord. The authors achieved 90 per cent survival of Stage I cases of this type. Roentgen therapy administered after previous irradiation failure was unsuccessful in all cases in which it was tried, but radiotherapy for recurrences following surgery resulted in 22 per cent cures (7 of 27 cases)

The authors make a plea for close cooperation between the laryngologist and radiologist in management of patients with carcinoma of the larynx. They feel it is possible that a revision and combination of surgical and radiation technics may result in more satisfactory results in advanced cases.

A brief note is given on the technic of treatment and reactions. In general, opposing 8-cm. circular lateral fields are used; h.v.l. 2.0 mm. copper; approximate minimum depth dose 4,700 r in four to five weeks. Moist desquamation was the usual skin reaction and healing occurred without incident. No instances of radionecrosis occurred in this series.

One diagram; 1 chart; 7 tables.

JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Laryngopharyngeal Cancer. Five-Year Results After X-Ray Therapy. C. C. Wang. New England J. Med. **255:** 1033–1035, Nov. 29, 1956. (Massachusetts General Hospital, Boston 14, Mass.)

This report is a statistical analysis of results in 150 cases of laryngopharyngeal ("extrinsic laryngeal") squamous-cell carcinoma seen over a twenty-year period, treated with conventional radiotherapy and followed for five years or more. Males predominated, 20 to 1, and the disease was most common after the age of fifty.

The tumors are divided into three groups: 29 anterior lesions (involving the epiglottis), which showed a 31 per cent five-year cure rate; 65 posterolateral (involving the arytenoid, aryepiglottic fold, pyriform sinus, or postcricoid region), showing only 12 per cent cures; 56 extensive tumors involving both anterior and posterolateral structures, with 17 per cent cures.

The cases are further subdivided into those with and without lymph-node involvement and on the basis of the size of the initial lesion. As might be expected, patients with cervical-node metastases showed considerably poorer survival rates than those with small localized lesions. Of the 150 patients, slightly more than half had lymph-node metastases at the beginning of therapy, and only 8 per cent of these survived for five years; 29 per cent of 72 patients in whom metastases were not evident at the time of treatment lived five years or longer.

The radiotherapeutic technic is briefly described. Conventional 200-kv radiation was used with added filtration of 0.5 mm. copper. The tumor was crossfired through two opposing lateral portals, 6 × 8 or 8 × 10 cm., for a depth dose of 4,500 to 5,000 r, at the rate of 200 r per day for a treatment time of five or six weeks. Occasionally an additional anterior portal was used.

Four tables. JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Squamous Cell Carcinoma of the Thoracic Esophagus. An Evaluation of Treatment Methods. Harry W. Burnett, Jr., and S. W. Moore. Am. J. Roentgenol. **76:** 949–955, November 1956. (525 East 68th St., New York 21, N. Y.)

A series of 64 proved cases of squamous-cell carcinoma of the thoracic esophagus followed for three or more years is evaluated from the following aspects: applicability, mortality, and end-results of surgical resection, radiotherapy, and combinations of the two. The data are extensively analyzed in chart and graph form in an attempt to determine what therapeutic measures will offer the majority of patients a maximum survival or comfortable palliation. Ten of the 64 patients had evidence of distant metastases before treatment was started and are excluded from further analysis. Of the remaining 54 cases, 48 were operated upon; in 39 thoracotomy was done, and in 9 only a gastrostomy. Of the 17 patients undergoing "curative surgery" (resection), 7 died in the hospital, a mortality rate of 41 per cent. In 4 of the "curative" surgical cases there was early recurrence, with subsequent radiotherapy. Thus only 6 patients actually received "curative" surgery as the only therapeutic approach; 3 of these were disease-free at three years.

Twenty-eight patients received roentgen therapy because they were judged unsuitable for operation, were found inoperable at thoracotomy, or were known to have residual tumor after resection. Seventeen were given what is considered an incomplete course of treatments, namely, a tumor dose of less than 4,500 r in four to six weeks. Inability of the patients to complete a rigorous course of radiotherapy was ascribed in most instances to debilitation following thoracotomy or an advanced stage of the disease with malnutrition.

Analysis of the data indicates the following:

(1) Irradiated patients with advanced unresectable lesions show a significantly higher percentage of survivals than surgical patients during the first year and a comparable salvage rate at two years. After the second year the surgical salvage rate is slightly higher, but still very low in overall percentage.

(2) Patients receiving adequate radiotherapy (tumor dose of 4,500 r or more) show a much better survival rate at all stages than those receiving inadequate irradiation or palliative surgery.

It is the authors' conviction that overall survival and palliation rate could be much improved if patients were treated primarily by adequate irradiation without preliminary thoracotomy. Most patients should be hospitalized during the treatment course for careful attention to nutritional and other supportive measures.

Four figures. JAMES W. BARBER, M.D.
Cheyenne, Wyo.

The Primary Treatment of Adenocarcinoma of the Rectum by High Voltage Roentgen Rays (1,000 kv). I. G. Williams and H. Horwitz. Am. J. Roentgenol. **76:** 919–928, November 1956. (St. Bartholomew's Hospital, London, England)

The treatment of choice for carcinoma of the rectum is surgery. When this is contraindicated by the advanced stage of the disease or for other reasons, high-voltage roentgen irradiation offers the patient an excellent chance of palliation and even a possible chance of cure.

In the management of the inoperable case, colostomy is indicated only when intestinal obstruction is present or imminent. If subsequent irradiation is contemplated, the colostomy opening should be a little higher than usual to avoid the treatment field.

The authors report a series of 189 cases which they classify as follows:

Stage I: Lesion confined to the rectal mucosa, not penetrating the rectal wall (8 cases).

Stage II: Lesion involving whole thickness of rectal wall but not extending beyond these limits.

Stage III: Spread beyond rectum to neighboring structures and/or involvement of regional pelvic nodes.

Stage IV: Carcinoma with distant metastases.

Treatment was by 1,000-kv roentgen rays (h.v.l. 9.3 mm. copper), the object being to deliver a tumor dose of 6,000 r in six weeks. With a cross-firing technic through five or six fields measuring 10 × 16 cm., it is possible to achieve a depth dose in the pelvis amounting to 120 to 140 per cent of the skin dose. The high kilovoltage results in equal distribution throughout the pelvis in spite of overlying bony structures. Dosage for the individual case must be planned and executed with care, and skilled nursing and supportive measures are of importance.

Results of treatment are assessed on the following basis: relief of symptoms due to the primary growth; avoidance of colostomy; avoidance of severe side-effects; survival. In the present series bleeding was partially or completely relieved in 90 per cent of the cases; pain in 77 per cent; tenesmus in 73 per cent; mucous discharge in 67 per cent. In general, relief of symptoms was proportional to shrinkage of the tumor. In 41 per cent of the patients colostomy was avoided.

In some 50 per cent of the series treatment had to be modified or interrupted because of immediate radiation reactions, but in no case did these represent a serious hazard. Late complications included fistulas in 6 per cent, chronic radiation necrosis in 5 per cent, and fibrosis with or without stricture of the rectum in 17 per cent of the cases. It is pointed out that the possibility of such serious effects must be faced if worthwhile results are to be obtained in a large percentage of cases.

The authors' survival figures are based on 165 cases treated between 1937 and 1949. These show 9 patients surviving five years, representing 5 per cent of the series. Six of these had since died (4 of intercurrent disease) and 3 were alive after eleven, twelve, and sixteen years. Two of the five-year survivors had Stage II disease and 7 Stage III.

Three photographs; 2 charts; 5 tables.

PAUL MASSIK, M.D.
Quincy, Mass.

Radium and X-Rays in the Treatment of Malignant and Benign Proctologic Diseases. Paul W. Scanlon. Am. J. Surg. **92:** 787–791, November 1956. (Mayo Clinic, Rochester, Minn.)

Selection of patients for radiotherapy for malignant lesions of the rectum and rectosigmoid must be carefully individualized. Although indications for irradiation of tumors of this region are limited, the author feels that significant degrees of palliation and an occasional cure merit consideration by all radiotherapists.

Carcinoma of the Rectum or Low Sigmoid: Patients with inoperable lesions, suffering from advanced tumor necrosis, bleeding, or discharge, can frequently be benefited by topical use of radium or radon plaques applied to the surface of the neoplasm per rectum. Because of

the rapid fall-off of radiation intensity with depth, surface doses of 5,500 to 7,500 r gamma can be safely given, often with considerable benefit to the patient. Higher doses, up to 11,500 r gamma at the surface, can be easily attained if a preliminary colostomy has been done and possible cicatricial stenosis is not a problem. With tumors invading the bowel wall and adjacent soft-tissue structures, supplemental external roentgen therapy may be a valid selection.

When perirectal extension of a rectal or rectosigmoidal neoplasm, with attendant pain and impairment of the neighboring viscera, or both, is the foremost problem, roentgen therapy may occasionally be useful; 3,000 to 4,000 r in fifteen to twenty-five days is the suggested tumor dose with conventional beam qualities. A higher dose, 4,500 to 5,000 r, can be tolerated with supervoltage technics. The number of patients suitable for such treatment is not great. In their selection, advantages to be gained by the more trying roentgen therapy must be weighed against the benefits of simple colostomy and general medical measures.

Smal non-infiltrating malignant polyps of the lower rectum may be treated by the application of radium plaques to the base of the lesion after preliminary fulguration. A surface dose of 11,000 r will result in a dose at 1 cm. depth of only 2,000 r.

Squamous-Cell Carcinoma of the Anus: Although the primary method of attack for favorably situated tumors of the anus is ordinarily surgical, there may be a place for intracavitary and interstitial radium therapy in some cases. For small, potentially resectable lesions in patients deemed inoperable for some other reason, the author employs an intracavitary anal dilator containing three 50-mg. tubes of radium, giving approximately 600 mg. hours in two sessions to the entire length of the anal canal. This delivers somewhat in excess of 3,000 r to the surface and more than 1,000 r at a depth of 1 cm. This, of necessity, must be supplemented by interstitially implanted radon seeds averaging 1 millicurie apiece, placed uniformly throughout the lesion and in an adequate surrounding margin. By this means, an additional dose of 5,000 to 6,000 r is delivered uniformly throughout the lesion. When the neoplasm extends much beyond the submucosal layers wide-field palliative roentgen or supervoltage therapy is indicated.

Brief comment is made on radiotherapy for benign anal and perineal conditions. Indolent, superficially infected postoperative wounds that are reluctant to heal will frequently show a favorable response to small anti-inflammatory doses of superficial radiation: 75 to 125 r two or three times weekly for a total dose of about 500 r are suggested. Pruritus ani and pruritus vulvae can be successfully treated on a similar dosage schedule, though routine use of x-rays for these conditions is deprecated. The problem here is one of ready relapse and the temptation to apply further radiations with possible ultimate overtreatment. While radiotherapy may be occasionally justified, careful selection is indicated.

Three tables. JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Review of Seventeen Years' Experience with Transvaginal Roentgen Therapy in Cervical Cancer. Ralph M. Caulk. Am. J. Roentgenol. **76:** 965–970, November 1956. (Garfield Hospital, Washington 1, D.C.)

A series of 733 patients with histologically proved carcinoma of the cervix receiving radiotherapy and followed for five or more years is reported. For purposes of analysis, 571 "determinate" cases are classified according to the League of Nations system. Five-year survival rates were 67 per cent, 36 per cent, and 17 per cent for Stages I, II, and III, respectively. There were no five-year cures of Stage IV cases. A group of 37 "modified" cases (*i.e.*, having had previous inadequate or unsuccessful treatment but subsequently given a definitive course of radiotherapy) showed a survival rate of 7 per cent. The total determinate cases are subdivided into groups according to the combinations of transvaginal roentgen therapy, external roentgen therapy, and radium therapy utilized, and each group is individually analyzed.

The largest category was that receiving external and transvaginal roentgen therapy only. For 304 determinate cases thus treated, the five-year survival rate was 40 per cent: 71 per cent for Stage I, 40 per cent for Stage II, 24 per cent for Stage III.

A group of 74 patients received external and transvaginal roentgen therapy with supplemental intracavitary radium. The results were esssentially the same as in the first group. It is felt, however, that radium is necessary as a supplement in those cases in which the disease has spread to the interior of the uterus. Supplementary radium is also indicated when the vagina is of such size that it can accommodate only a small transvaginal speculum.

A third small group (20 patients) received transvaginal roentgen irradiation and intracavitary radium as their only form of treatment. This method was selected for very obese patients for whom external therapy was not felt to offer great benefit. Generally only Stage I and II lesions were so treated, showing relatively low survival rates, 58 and 16 per cent respectively.

In 80 cases treatment was limited to transvaginal roentgen therapy. In carefully selected Stage I and early Stage II cases, five-year survival rates were 68 and 12 per cent, respectively. Such treatment was selected only for patients whose vaginas could accommodate large or fairly large specula and in whom the tumor appeared to be well localized to the cervix proper.

A sixth group, numbering 93, received no transvaginal irradiation. These tended to be less favorable patients, with more advanced disease and small vaginas unable to tolerate transvaginal specula. Results were relatively poor: 43 per cent, 19 per cent, and 5 per cent five-year survivals in Stages I, II, and III, respectively.

Complications of these various combinations of therapy are summarized briefly. The only important one appears to be rectal ulceration and stricture. This appeared in 4 of 44 carefully studied cases and required surgical resection. Some lesser degrees of rectal difficulty were managed without surgical intervention. It appears that the complications described result from supplementary external roentgen irradiation rather than from the transvaginal therapy *per se*. It is the author's philosophy that a 10 per cent incidence of a surgically correctable complication is a justifiable calculated risk in aggressive management of a serious disease. JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Treatment of Malignant Lymphoma and Blood Dyscrasias by Conventional Roentgen Therapy. H. B. Elkins. Am. J. Roentgenol. **76:** 960–964, November 1956. (University Hospitals, Iowa City, Iowa)

Roentgen therapy is still felt to be the basic modality

of treatment for malignant lymphomas and blood dyscrasias, even though new therapeutic tools are frequently helpful or preferable in selected cases. The author presents only a basic plan for management of these multiple diseases and stresses individual consideration of each patient as of paramount importance.

In *Hodgkin's disease*, lesions localized to a single lymph node or juxtaposed groups of nodes are treated with moderately heavy roentgen therapy, 3,000 to 3,500 r tumor dose in ten to fourteen days. This treatment appears to be the most effective in attaining a long-term survival, although there are confusing exceptions. Many cases are known where a very small roentgen dosage has resulted in long-term control. Widespread disease is managed with the smallest dose compatible with relief of symptoms. Cases showing systemic manifestations frequently do not respond well to roentgen therapy, and it is in this group that chemotherapy is most likely to be helpful. Occasionally small doses of total-body irradiation are helpful.

In *malignant lymphoma*, a wide divergence of roentgen responses is encountered. On the face and scalp, tumors of the reticulum-cell type may respond to as little as 400 r (air); in the orbit, tongue, and antrum, 2,500 to 3,000 r given over a period of ten to fourteen days may produce long-term remissions, while retroperitoneal lymph nodes may prove radioresistant. In generalized disease, minimal effective doses to troublesome node masses should be used.

In *blood dyscrasias*, the symptoms are believed by the author to be a more reliable guide to treatment than the white blood cell count per se. Many dyscrasias can be controlled for a variable time by roentgen therapy alone.

Patients with *lymphatic leukemia* whose only complaints are referable to enlarged nodes should be managed with small, gentle courses of roentgen therapy confined to the involved areas. Individuals showing quite high white cell counts or systemic symptoms frequently benefit from small doses of total-body or half-body irradiation. In general only enough radiotherapy is given to control symptoms.

In the majority of cases of *myelogenous leukemia*, symptoms arising from splenomegaly are the most prominent and can usually be satisfactorily managed by small doses of radiation to the spleen. In these instances the amount of therapy should be judged by the behavior of the spleen as it shrinks and by the associated blood cell counts. JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Spontaneous Course of Cervical Precancerous Conditions. Olaf Petersen. Am. J. Obst. & Gynec. **72**: 1063–1071, November 1956. (Radium Center, Copenhagen, Denmark)

This study is based on 127 patients seen from 1930 to 1950 with a histologic diagnosis of precancerous cervical lesions, followed but without treatment during the observational period. The series does not represent retrospective selection but the cases from the outset were recognized as precancerous. The total number of such cases seen during the period was 212; 85 were treated owing to various circumstances not directly related to the histology.

All the 127 untreated patients have been followed for three years, 82 per cent for five years, and 30 per cent for a minimum of ten years. After one year manifest carcinoma of the cervix had developed in 4 per cent; after three years in 11 per cent; after five years in 22 per cent, and at the end of nine years in 33 per cent. Of the 34 patients in whom carcinoma developed during observation, 26 were alive without recurrence, with 2 dying free of disease. Actually only 6 patients died of carcinoma during this follow-up. Five of the 7 patients with late Stage II to IV disease had waited from two to more than eight years to return for follow-up.

The author feels that patients with precancerous lesions of the cervix (epithelial hyperplasia with nuclear abnormalities and/or borderline cases of suspicious or incipient invasiveness) do not present an acute problem and that it is justifiable to temporize if the patient can be kept under regular control, *e.g.*, examination every two or three months, new biopsies, and cytological examinations. If such a follow-up cannot be carried out, total hysterectomy is preferred to radium application.

Six figures; 2 tables. ROBERT L. EGAN, M.D.
University of Texas, Houston

Basal-Cell Carcinoma of the Vulva. R. C. Ackles and J. P. Pratt. Am. J. Obst. & Gynec. **72**: 1124–1126, November 1956. (Henry Ford Hospital, Detroit 2, Mich.)

Among 31 cases of carcinoma of the female external genitals seen during the past thirty years there were 2 cases of basal-cell carcinoma, both on the vulva. Among 182 cases of carcinoma of the vulva collected from the literature, including the present series, there were 13 basal-cell carcinomas, a 7 per cent incidence. It is felt, however, that the actual incidence cannot be stated because of the infrequent appearance of the disease.

Wide local excision is suggested as the logical surgical approach.

One photograph; 1 microphotograph.
ROBERT L. EGAN, M.D.
University of Texas, Houston

Preoperative Irradiation. A. Zuppinger and H. R. Renfer. Radiol. clin. **25**: 384–408, November 1956. (In German) (Röntgeninstitut der Universität und des Inselspitals Bern, Bern, Switzerland)

Radiobiologic considerations lead to the conclusion that today preoperative irradiation technics represent in general the most effective therapeutic principle in combined tumor therapy. The advantages are envisioned in the possibility of converting an inoperable or a questionably operable tumor into an operable one through shrinkage. Though the surgical approach may be made more limited in the operable tumors by preoperative irradiation, the standard operative procedures are recommended. One may expect a diminution of the propagation of the tumor at operation, with a lowered tendency to recurrence and distant metastasis.

The disadvantages of preoperative irradiation are limited to occasional disturbances in wound healing and the prolongation of the total treatment time. These can be minimized by proper dosage and the appropriate choice of time for the operative attack, as well as the correct psychologic preparation of the patient.

The principle of preoperative irradiation has been proved in the management of cancer of the breast. Details are given concerning dosage, method of irradiation, time of surgery, influence of biopsy, etc. The procedure has also led to improvement in the results ob-

tained in mixed tumors of the kidney, carcinoma of the upper jaw, and high rectal cancers. In all of these, preoperative irradiation should be considered as the therapy of choice.

Because of the poor results in carcinoma of the bronchus and stomach, much more extensive trials with preoperative irradiation are indicated; the prospects in these heretofore practically hopeless tumors are today more favorable than even a short time ago, because the problem of the necessary depth dose can be regarded as solved (rotation therapy and supervoltage).

The extension of preoperative irradiation to other types of tumors is to be regarded as the most suitable measure today for improving our results in the fight against cancer.

All radiotherapists and surgeons who deal with cancer should read this article in the original.

Fourteen roentgenograms; 1 photograph; 1 graph; 8 tables.

CHRISTIAN V. CIMMINO, M.D.
Fredericksburg, Va.

Clinical Aspects of Betatron Irradiation. Lewis L. Haas and Roger A. Harvey. Am. J. Roentgenol. **76:** 905–914, November 1956. (L. L. H., University of Illinois Hospital, Chicago, Ill.)

This report is based upon the treatment of 180 malignant tumors with 23-MEV betatron radiation, which has the usual advantages of high energy radiation, namely, higher depth dose with less skin damage. The difficulty with this form of radiation is that the time-dose relationships have not yet been fully worked out.

The series reported included 83 deep-seated lesions, in the lungs, esophagus, digestive organs, and genitourinary tract; 59 less deeply-seated lesions, in the brain, spine, nasopharynx, oropharynx, and larynx; and 38 cases of advanced disease treated by spray irradiation technics.

Fifty-one lung cancers were treated, 9 of which were of the Pancoast variety. In this latter group, 1 patient was alive and well at the time of the report, seventeen months after treatment, and 4 had died of unrelated causes in periods up to four years. The other pulmonary tumors were varied, and their responses were as usual. Eighteen esophageal cancers were included in the series, with results approximately as good as those to be expected from surgery. Radiation damage to the normal tissues was the major cause of difficulty. Nearly all the cases were far advanced or inoperable. One patient remained alive and well two years after treatment.

The result of betatron therapy of the less deeply situated lesions in the head and neck was approximately the same as with lower voltage radiation. The chief advantage here was that less cartilage and bone damage occurred. Few abdominal or genitourinary cases were treated.

The third group of patients treated for widespread or generalized cancer showed better cancer control, but more damage to the normal surrounding tissue occurred.

The authors conclude that "administration of an adequate higher tissue dose occurs in a relatively greater number of patients under megavoltage regimen than with conventional methods." They believe that there is a very definite place for betatron therapy in clinical cancer management, its advantages being largely related to spatial distribution of dose. The risks of late radiation damage are not out of proportion to those encountered in adequate conventional therapy. It is believed that they can be reduced with further work in the field of optimal time-dose relationships.

Twenty roentgenograms; 1 table.

PAUL MASSIK, M.D.
Quincy, Mass.

A Clinical Program to Evaluate the Practical Significance of Higher Energy Levels Than the 1-3 Mev. Gilbert H. Fletcher. Am. J. Roentgenol. **76:** 866–893, November 1956. (M. D. Anderson Hospital, Houston 25, Texas)

A program of comparative evaluation of a kilocurie cobalt-60 teletherapy unit with a 22-MEV betatron has been under way for a number of years at the M.D. Anderson Hospital, Houston, Texas. The cobalt unit is equivalent in its physical characteristics to the 3-MEV roentgen-ray generator but differs in the geometric shape of the beam. The x-ray beam has little if any penumbra and a sharp cut-off, so that it is well suited to rotation therapy. The penumbra of the cobalt-60 beam is also minimal at 50 cm., but at 70 cm., the usual distance for rotation technics, it becomes considerable, and the fall-off is smooth, resulting in high dosage to large volumes of tissue and a large integral dose in the slab of the body in which the tumor is located, with consequent intolerance to treatment.

The physical properties of the 22-MEV betatron differ substantially from those of the 1- to 3-MEV roentgen-ray generators in the much deeper electronic build-up, and the significantly increased depth dose. There is also a lack of side-scatter or penumbra. At the higher energy levels, the "hot spots" in the subcutaneous tissue can be eliminated and the tumor dose is markedly increased. The volume distribution is optimal within the tumor-bearing area and very favorable outside of it.

For the comparative study described here, a number of tumors in different body sites were selected. Generally speaking the cases were potentially curable, *i.e.*, still localized to the primary site or with metastases to the proximal lymph nodes only. Included were advanced tumors of the oral cavity and larynx, the posterior third of the oral cavity and pharynx; late squamous-cell cancers of the cervix; and infiltrative cancers of the urinary bladder. Some squamous-cell cancers of the esophagus were also treated because of the ease of check-up. The allocation of material to one type of therapy machine or the other was based upon the possibility of delivering the desired tumor dose, without overtaxing normal tissues, by simple, reproducible, and anatomically accurate settings. When the volume distribution was equally satisfactory for both pieces of equipment, cases were alternated.

The clinical experiment was started by keeping constant tumor dose and time for the same clinical entities, in order to obtain information on tumor response, mucous membrane reactions, whole-organ tolerance, and total-body tolerance.

The results obtained in the various groups of tumors mentioned above are discussed at length. Head and neck tumors in general received 6,000 r (tumor dose) in four weeks if they required less than 80 sq. cm. surface coverage; when a larger field was necessary, the time was prolonged. The results were essentially the same for cobalt-60 and betatron irradiation in this group, both in respect to the production of mucositis and tumor regression. The incidence of primary regression was much higher than in similar groups of

cases treated with conventional technics. A high incidence of clinical disappearance of involved lymph nodes was also obtained.

Results in cancer of the esophagus were very poor. Treatment of cancer of the urinary bladder was more encouraging. Here the dose was 6,000 r in five weeks. The results with both modalities were better than with medium kilovoltages. The betatron treatments seemed to be somewhat better tolerated.

One hundred and fifty late Stage II and Stage III cancers of the cervix were treated, with an attempt to deliver 6,000 r to the pelvic walls in six weeks. When it was found that this dosage with the cobalt unit resulted in severe radiation reactions, betratron therapy was used in all cases. This was followed by radium application for 3,000 mg. hours (Manchester technic). The optimum dosage has not yet been determined.

While the details of dosage and technics require further study, certain observations of significance have been made. The clinical radiobiological effectiveness (RBE) is seemingly 1 between cobalt 60 and 22-MEV betatron radiation for epithelitis of the soft palate. It is 0.8 to 0.9 between roentgen rays of 3 mm. Cu h.v.l. and the cobalt-60 and 22-MEV betatron rays. In the whole pelvis technic, using as a test small bowel irritation (diarrhea), 600 to 700 r per week with roentgen rays (h.v.l. 3 mm. Cu) are as well tolerated as 1,000 r with the units used in the present study (stationary portals), an RBE of 0.65.

As the volume irradiated increases, the same number of roentgens are seemingly better tolerated with the betatron than with the cobalt unit. If the doses are expressed in rads, the 22-MEV rad is apparently more effective than the cobalt-60 rad, but for large-volume irradiation the two appear more nearly equal.

An Appendix by W. K. Sinclair considers dosimetry and relative biological effectiveness from the physicist's point of view.

Forty figures; 1 table. PAUL MASSIK, M.D.
Quincy, Mass.

Field Localization for Betatron Therapy. Jasper E. Richardson, Earl Van Roosenbeek, and Jack M. Morgan. Am. J. Roentgenol. **76:** 934–938, November 1956. (J. E. R., Shell Development Co., Houston, Texas)

A field localizing device utilizing mirrors and lights has been developed for use with the Allis-Chalmers 24 RCM betatron in use at the M. D. Anderson Hospital, Houston, Texas. Construction specifications of the light localizing unit are described. The unit is fitted into place on the machine in the same manner as the treatment cones supplied by the manufacturer. The localizer must be removed before treatment is begun.

On experimentation with filming of the treatment field with the localizer and patient in place for therapy, it was found that special high-contrast, fine grain films with lead intensifying screens were needed. The resulting films are satisfactory for verification of field localization, although their contrast is low. Factors for betatron film exposures are given in graph form.

Four figures. JAMES W. BARBER, M.D.
Cheyenne, Wyo.

An Automatic Field Mapping Device. R. J. Schulz. Am. J. Roentgenol. **76:** 939–941, November 1956. (Memorial Center, New York, N. Y.)

A device is described which makes possible rapid determination of field intensity plots for various types of radiotherapy machines. Essentially the unit consists of a detector probe attached to a movable carriage. A system of servo (selsyn) motors transmits movement of the carriage within the radiation beam to a battery of charts and electronic recorders in the control room. With this device the intensity within any therapy field can be quickly and accurately mapped.

Two photographs; 1 diagram.

JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Effect of Oblique Filtration in Radium Dosimetry. R. G. Mitchell. Brit. J. Radiol. **29:** 631–632, November 1956. (Radiotherapy Department, General Hospital, Northampton, England)

In the Paterson-Parker radium dosage system it is assumed that the obliquity of filtration toward the end of a linear source is of no practical significance. This assumption the author put to test by calculating the dosage from an unfiltered source and making appropriate reduction for any filtration (neglecting effect of obliquity) and comparing this to the Sievert table data for that particular filtration (including effect of obliquity). This was done for a variety of Paterson-Parker planar distributions and it was found that the dosage error 0.5 cm. beneath the mid-point of the source increased significantly as the elongation factor grew greater when oblique filtration was taken into account. The following correction factors to include the effect of oblique filtration are suggested for calculating minimum dose.

Elongation	Multiply per cent error by
2/1	1.1
3/1	1.2
4/1	1.3

No correction is necessary for oblique filtration in circular distributions. G. M. STEVENS, M.D.
Palo Alto, Calif.

Fast Neutron Dosimetry at the Argonne National Laboratory Cyclotron. Richard B. Rhody. Radiation Res. **5:** 495–501, November 1956. (Radiation Research Laboratory, College of Medicine, State University of Iowa, Iowa City, Iowa)

The neutron dose from a cyclotron, as delivered to an animal exposure facility, has been measured by four different methods. The independent measurements were made by personnel from Columbia University, Oak Ridge National Laboratory, the U. S. Naval Radiological Defense Laboratory, the School of Aviation Medicine, the State University of Iowa, and Argonne National Laboratory. Tissue-equivalent ionization chambers, fast neutron proportional counters, threshold detectors, thimble chambers, and chemical dosimeters were used to measure the neutron dose rates.

The neutrons were produced by the bombardment of a thick beryllium target with 21-MEV deuterons. Animals were exposed inside 3-inch lead wall enclosures as part of a neutron-induced cataract study. These enclosures were located in the forward neutron beam and at 180° to this beam. The dosimeters were placed in the normal animal positions.

The agreement among the dosimetry methods was excellent, with an average deviation of only 8 per cent in the direct beam and 4 per cent at 180°.

Earlier monitoring of the neutron dose was done with thimble chambers using the n as the unit of measurement. The measurements made in this study give a calibration factor for these chambers of 1.5 rep/n.

Four tables. AUTHOR'S ABSTRACT

RADIOISOTOPES

Radioactive Tracers in Radiobiological Studies. The Thirty-sixth Silvanus Thompson Memorial Lecture. G. C. Hevesy. Brit. J. Radiol. **29:** 465–477, September 1956. (Institutet für Organisk Kemi och Biokemi, Stockholms Hogskola, Stockholm, Sweden)

The greater part of this paper is concerned with the effect of irradiation on the rate and amount of desoxyribonucleic acid formation in organs and tumors. The DNA is quantitated according to the amount of P^{32} and C^{14} incorporated into the DNA molecule.

There is a concurrence of experimental observations that the rate of DNA formation is depressed following irradiation. A discussion of how and why this effect is produced is given. It would appear that depression of DNA synthesis is a sequel of general cell damage.

DNA synthesis in relation to the mitotic cycle is discussed and experimental work along this line is cited. The hypothesis that ionizing irradiations interfere with DNA synthesis by breaking chemical bonds is offered.

The striking correlation existing between radiosensitivity of organs and the turn-over rate of DNA is pointed out. In general, the more rapid the turnover, the greater the radiosensitivity.

Hematopoietic depression following irradiation is discussed and experiments are cited indicating that this is due to interference with the incorporation of Fe^{59} into hemoglobin. This interference with hemoglobin formation is attributed to the radiation sensitivity of the marrow cells. Radiation produces mitotic arrest in the latter, new formation of erythropoietic cells is hindered, and, if larger doses are applied, cell destruction independent of mitotic processes may take place as well. Cell death may be independent also of interference with the DNA molecule, since it has been shown that the physiological death rate of the mammalian red corpuscle not containing DNA may be accelerated by exposure of the organism to radiation.

Experimental evidence obtained with radiophophorus as a tracer shows that growth in one organ or tumor promotes DNA formation in other organs. From this point it is hypothesized that tumor promotes its own growth and predisposes to the formation of other neoplastic tissue.

This paper in which, according to the author's own statement, facts and hypotheses are intermingled, does not lend itself to abstracting. It should be read in the original by those interested in the problems it discusses.

Thirteen figures; 2 tables.

THOMAS P. MOORE, M.D.
Bowman Gray School of Medicine

Treatment of Thyrotoxicosis with Radioactive Iodine (I^{131}). Keith D. Fairley, W. P. Holman, and W. E. King. M. J. Australia **2:** 701–710, Nov. 10, 1956. (Royal Melbourne Hospital, Melbourne, Australia)

The results of treatment of thyroid disease are considered under the following headings: diffuse toxic goiter; postoperative recurrent diffuse toxic goiter; nodular toxic goiter. Operation remains the treatment of choice for the nodular goiters, but in the other two groups is being replaced by treatment with I^{131}.

Diffuse Toxic Goiter: Sixty-four patients who had had no previous treatment with I^{131} were studied. A "basic dose" of 6 or 7 mc I^{131} was given in one drink. This dose was increased by 1 or 2 mc if the goiter was of more than "moderate" size. For patients with previous uptake studies showing greater than 70 per cent twenty-four hour retention in the thyroid, the dose was decreased by 1 mc and in those with retention of less than 50 per cent it was increased by 1 or 2 mc. Earlier in the series the dosage was modified mildly if the degree of clinical thyrotoxicosis was severe, but later experience indicated that such modification for this reason was not indicated. Following experience the "basic dose" of 7 mc was selected over smaller doses of 5 or 6 mc.

Postoperative Recurrent Thyrotoxicosis: Eleven patients were treated in this group. Again the basic single oral dose was 7 mc. Mild dose modification of 1 or 2 mc, more or less, was utilized for patients showing very high or moderately low uptake studies at twenty-four hours.

Toxic Nodular Goiter: Seventeen cases were treated in this group. A basic dose of 15 mc was arrived at. For large glands with multiple nodules, the dose was increased to as much as 20 mc. The results of treatment and all untoward effects are analyzed in tedious detail. Numerous short case histories are given.

The conclusions as to indications for radioactive iodine treatment of thyrotoxicosis are, in general, very similar to those given by others. Clinical results were generally good. It is pointed out that excessive or prolonged use of antithyroid drugs after I^{131} therapy may result in temporary hypothyroidism and an increase in the size of diffuse goiters. Such drugs should be omitted, therefore, whenever possible, and should rarely be used for longer than six weeks following radioiodine therapy.

The authors feel that their simple determination of required oral dose is adequate in the vast majority of cases and that more complicated calculations are generally unnecessary. Further, they believe that diffuse toxic goiter can be treated satisfactorily in most instances without any knowledge of the retention of iodine by the gland as determined by uptake studies. The point is made that in cases of toxic nodular goiter managed by I^{131} the risk of subsequent hypothroidism is negligible.

In this series it was noted that fertility in female patients showed a pronounced increase after return of normal thyroid function.

Five tables.

JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Some Observations on the Clinical Effects of Cobalt-60 Telecurie Therapy. C. C. Burkell and T. A. Watson. Am. J. Roentgenol. **76:** 895–904, November 1956. (City Hospital, Saskatoon, Saskatchewan, Canada)

The authors report the results of four years of Co^{60} therapy at the Saskatoon Cancer Clinic (Saskatchewan), where it was used routinely in cases that would previously have been treated by 400-kv roentgen rays. The cobalt apparatus is easy to use, and in general provides a higher tumor dose than conventional equipment. Since the maximum reaction occurs about 4 mm. below the skin surface, open-ended cones without bolus are used. For the usual case fifteen to twenty-five doses are given in a three- to five-week period. All types of lesions were treated.

Breast: Postoperative therapy was instituted for all

lesions of the inner half of the breast, and in other cases only if axillary metastases were present. A central tumor dose of 4,200 r to the axilla and a similar dose to the parasternal area were found to be most satisfactory. In 46 per cent of the cases pulmonary changes of varying degrees of severity developed. Reactions were more severe if the parasternal field was used.

Larynx: Two right-angled fields measuring 5 × 5 or 7 × 5 cm. with a wedge filter near the apex were used in the treatment of intrinsic laryngeal tumors. A tumor dose of 6,000 r was given in five weeks. The skin tolerated this treatment well. Among 8 cases of extrinsic cancer of the larynx there were 3 survivals. For these cases, 10 × 10 cm. opposing fields were used, with a tumor dose of 6,000 r in five weeks. This resulted in a severe mucosal reaction.

Cancer of the Maxillary Antrum: In early cases of cancer of the maxillary antrum radium is preferred. In later cases where the wall was involved, Co^{60} was employed, with right-angled fields, wedge filters, and a dose of 6,000 r in five weeks. If necessary, the eye was included in the field. The tissue and mucosal reaction was slight.

Cancer of the Cervix Uteri: The initial treatment for cervical cancer was radium application according to the Manchester technic, with delivery of 7,000 r to point A. After this, Co^{60} was used to deliver 3,250 r to point B. Parallel 12 × 10 cm. anteroposterior and posteroanterior portals were used, separated by a 4-cm. thick lead block measuring 4 × 10 cm.

Superficial Carcinoma: Because of the lower absorption of high-energy radiation by bone and cartilage, Co^{60} is useful for treatment of superficial neoplasms, especially of cartilage and bone. A number of lesions of the ear, nose, and eyelids were treated. In order to achieve a 100 per cent surface dose, 3 mm. of Lucite were used to cover the end of the applicators. The dose was generally 6,000 r in three weeks. Results were good. No cartilage necrosis resulted.

Urinary Bladder: Of 21 patients treated for carcinoma of the bladder, 8 had died and 13 were alive (3 with residual cancer). All cases were far advanced so that the only alternative was total cystectomy. Horizontal rotation, with an 8.4 to 9.6 cm. square portal, was used. The total dose was 5,500 r in nineteen days to 7,200 r in thirty-eight days.

Lung: Twenty-three inoperable cases of pulmonary carcinoma were treated, either with rotational or large-field technic. The dose with rotational therapy was 4,000 r in seventeen days. The dose for large fields (10 × 15 or 15 × 15 cm.) was 5,500 r in thirty-five days. Smaller fields allowed the administration of 6,500 r in thirty-two days. The longest survival was two and a half years. Of 23 patients, 15 died and 8 were still alive. All patients received nitrogen mustard prior to the start of treatment, since it appears to have a synergistic effect.

Metastases: Co^{60} proved to be equally satisfactory for soft-tissue and bony metastases. In spite of the lesser absorption of high-energy radiation by bone, the surrounding soft tissue received a higher dose, with generally more beneficial effects. The factor of greater penetration also makes Co^{60} particularly valuable in treatment of lesions which are adjacent to or covered by bone.

Eleven roentgenograms; 4 diagrams; 1 table.

PAUL MASSIK, M.D.
Quincy, Mass.

Early Experiences in the Treatment of Carcinoma of the Uterine Cervix with Cobalt^{60} Teletherapy and Intracavitary Radium. James F. Nolan, Juan A. Vidal, and John H. Anson. Am. J. Obst. & Gynec. **72:** 789–803, October 1956. (Los Angeles Tumor Institute and the University of Southern California, Los Angeles, Calif.)

From July 1953 to July 1955, 50 patients with carcinoma of the cervix were treated with 1,000-curie Co^{60} teletherapy apparatus and intracavitary radium. A comparison was made with 197 primary patients treated during the preceding five years with essentially the same technics, but differing in that a 450-kv x-ray apparatus (5 mm. Cu h.v.l.) was used for the external therapy. Dosage and time of delivery to points A and B were in keeping with modern concepts of treatment. By studying 50 matched patient-pairs representing all stages of the disease, the authors felt that, even after a relatively short follow-up, some observations could be made: Results were slightly superior in the Co^{60} series, this superiority being related to a more uniform distribution of radiation throughout the parametrium.

The greater ease with which parametrial dosage may be raised with supervoltage sources suggests modification in treatment plan for only moderate increase in external irradiation in early cases, but an appreciable increase in advanced cases, with limitation of the dose from intracavitary radium (an established practice in some institutions).

Seven figures.

ROBERT L. EGAN, M.D.
University of Texas, Houston

The Use of Tantalum 182 in the Treatment of Early Bladder Carcinoma. P. J. van Miert and J. F. Fowler. Brit. J. Radiol. **29:** 508–512, September 1956. (Royal Victoria Infirmary, Newcastle upon Tyne, England)

The current methods of treatment of bladder carcinoma are briefly discussed, with emphasis upon the mortality and morbidity of radical and partial cystectomy. For lesions of moderate size, confined to the bladder, the authors consider irradiation to the whole organ unjustifiable, particularly in view of the complications incident to effective dosage. If, however, high irradiation dosage to the lesion-bearing area is achieved with minimum exposure of the unaffected bladder areas, a marked rise in cure rates can be expected. The use of tantalum-182 wires is an improved means of accomplishing this end. Two methods of interstitial bladder implantation with tantulum 182 are described.

The first method recommended is implantation from within the bladder lumen. Slotted needles with stilets are inserted under the lesion between the muscle and mucosal layers. The tantulum wires are then inserted into the needles and displaced *via* the longitudinal slots into the desired treatment area or areas. Withdrawal threads attached to the wire afford means of removal following the treatment period. The bladder incision is closed around an inflated balloon catheter, thus lowering the dose to non-implanted portions. Stereoscopic films are taken for assessment of the dose rate.

The second method consists in interstitial implantation from the external bladder aspect, in association with partial cystectomy. This procedure is used to avoid the suprapubic catheter track passing through the area of high dosage. Following excision of the lesion-bearing area, a stab wound is made to one side of the incision for palpation and guidance of the introducing needles. The remainder of the procedure is as de-

scribed above. This method is also recommended for implantation without partial cystectomy for treatment of fundal lesions.

Two illustrative cases are presented.

Five figures.

DAVID H. NEWBERN, M.D.
Bowman Gray School of Medicine

Experimental Studies on Interstitial Injection of Radioactive Colloidal Gold (Au^{198}). Andrew H. Veldhuis, Laymond A. Swinehart, Luther E. Preuss, and C. Paul Hodgkinson. Surg., Gynec. & Obst. **103**: 539–551, November 1956. (Henry Ford Hospital, Detroit 2, Mich.)

In an experiment designed to investigate the behavior of radioactive colloidal gold injected interstitially, the authors utilized rabbits weighing between 3,600 and 4,500 grams. The site selected for injection was the left inferior thoracic mammary gland.

The project was divided into three phases: the first phase was characterized by the injection of 4 per cent direct sky-blue colloidal dye solution, the second phase by the injection of non-radioactive colloidal gold solution with and without hyaluronidase, and the third by injection of colloidal Au^{198}.

It was found that the sky-blue dye particles migrated to the regional lymph nodes more rapidly than the colloidal gold particles, but that the sequence of distribution to various node areas and the relative concentrations attained were similar to those following injection of colloidal gold. The data showed that, in the rabbit, lymphatic drainage from the left inferior thoracic mammary gland occurs in the following order: left internal mammary lymph nodes, left axillary lymph nodes, right corresponding breast, right internal mammary lymph nodes, and right axillary lymph nodes. On a quantitative basis, the percentage of colloidal gold which traversed the mid-line to gain access to the contralateral organs averaged about 20 per cent of that localizing in the ipsilateral nodes. Likewise, hematogenous spread occurred promptly following the injection, but the order of magnitude was about 1 per cent of the amount of the colloid deposited in the lymph nodes.

The regional lymph nodes in all of the rabbits studied showed a high percentage of specific concentration of the radioactive gold. Gold was present in all of the nodes, both ipsilateral and contralateral. The concentration was particularly high in the ipsilateral nodes. For homogeneous distribution in the regional nodes the breast must be homogeneously infiltrated with volumes of solution equal to 1 c.c. per gram of tissue.

The initial transport of the gold colloid from the breast was very rapid; more than 80 per cent of the dose left the breast in forty-eight hours. Severe local reactions are thus avoided. The early transport of the isotope from the breast was reflected in the percentage of specific concentration built up in other tissues. The investigation showed that the maximum radiation was delivered to the regional nodes. The concentration here, on the basis of calculated dose, indicates a new order of magnitude in terms of radiation dosage. Examination of sections of the nodes revealed micropathological changes which were more pronounced than are produced by external radiation.

Seventeen photomicrographs; 9 graphs.

JAMES E. BAUER, M.D.
University of Missouri

The Stability of Radioactive Iodinated Serum Albumin Preparations in Man. H. J. G. Bloom, D. J. Crockett, R. P. Ekins, E. M. Ledlie, D. M. Taylor, and P. S. Vassar. Brit. J. Radiol. **29**: 585–587, November 1956. (H. J. G. B., Meyerstein Institute of Radiotherapy, Middlesex Hospital, London W. 1, England)

In an effort to evaluate the uniformity and stability of various preparations of radioiodine-labeled human serum albumin (RISA) made in England, and the Abbott preparation made in the United States, the authors followed the plasma activity at intervals after injection and also calculated the per cent of urinary excretion in small numbers of patients, each of whom received one of the three forms of RISA investigated. Because of relatively rapid diffusion of labeled albumin into the extravascular albumin pool, the urinary excretion rate probably gives the more accurate indication of RISA stability. The twenty-four-hour excretion varied between 3 and 73 per cent among the various preparations in normal persons, indicating the qualitative variation in the preparations tested and showing the limitation of their value in experimental protein turn-over research. Numerous tests failed to disclose the definite cause of this instability. The authors' experience, on the other hand, confirms the reliability of plasma volume studies using RISA by their good correlation with a simultaneous dye-dilution study. Some success had been achieved by the RISA preparation centers in producing a more stable product.

One graph; 2 tables.

G. M. STEVENS, M.D.
Palo Alto, Calif.

RADIATION EFFECTS

Radiation Doses to Patients and Personnel in Modern Roentgen Diagnostic Work. Lars-Eric Larsson. Acta radiol. **46**: 680–689, November 1956. (Karolinska Sjukhuset, Stockholm, Sweden)

In this report emphasis is given to the fact that radiation doses may become quite high during diagnostic roentgen examinations. By means of direct r-meter measurements on patients, department personnel, and dummies, it was found that doses exceeding 100 r are not uncommon with certain examinations. Patient exposure is greatest during fluoroscopy, the higher doses being received during such examinations as cardiac catheterization and angiocardiography, body-section radiography of the lumbar spine, and bronchography.

Personnel doses, as shown by hip-pocket and chest r-meter readings, seem quite safe for most conventional radiographic procedures. However, doses to the hands of attendants and personnel often approach those received by the patient, and radiation risks depend primarily upon work habits and protective efforts.

The point is stressed that dose rates during fluoroscopy have to be found by individual measurement. The radiologist must realize that magnitude of patient exposure is sometimes comparable to that in radiotherapy, and it is necessary to be able to calculate the dose.

Five figures; 3 tables.

DON E. MATTHIESEN, M.D.
Phoenix, Ariz.

Some Measurements of Scattered Radiation from Roentgen Diagnostic Beams. Jon Flatby and Sem Maudal. Acta radiol. **46:** 690–699, November 1956. (State Institute of Radiophysics, Oslo, Norway)

This study of scattered radiation was directed particularly to the area adjacent to the fluoroscopic screen of a diagnostic x-ray unit. By using a "hardboard" phantom and several ionization chambers, numerous measurements were made with and without lead-rubber side screens hanging from the edge of the fluoroscopic screen. In this experimental installation a concrete wall was present about 50 cm. to the right of the screen, and readings were taken with and without an iron plate covering that wall.

Observations indicated that the side-screens effectively reduced dose in the shaded area, and reduced considerably the amount of scatter from the concrete wall. In addition, it was shown that covering the wall with iron (which is more highly absorbable than other ordinary elements) further reduced the secondary radiation about the room.

Six figures. DON E. MATTHIESEN, M.D.
Phoenix, Ariz.

Thyroid Cancer in Childhood and Adolescence. James D. Majarakis, Danely P. Slaughter, and Warren H. Cole. J. Clin. Endocrinol. **16:** 1487–1490, November 1956. (University of Illinois College of Medicine, Chicago, Ill.)

Fifteen cases of cancer of the thyroid occurring between the ages of five and twenty years are reported. This number included 7 papillary adenocarcinomas (46.6 per cent), 5 adenocarcinomas (33.3 per cent), and 3 adenocarcinomas in adenoma (adenoma malignum) (20 per cent). The authors' figure for the incidence of carcinoma in non-toxic nodular goiter in children is 31 per cent, which is in good agreement with those reported by others.

A very definite point is made of the fact that all of the 10 patients fifteen years of age or under had received x-ray therapy to the head or neck in infancy or early childhood for one or another reasons, with dosage varying from 200 to 625 r. It is strongly suggested that the irradiation had something to do with the high incidence of carcinoma of the thyroid in this group. None of the 5 patients between the ages of sixteen and twenty gave a history of any previous irradiation.

One table. CHARLES E. DUISENBERG, M.D.
Palo Alto, Calif.

Radiation Cancer and Jean Clunet. Piero Mustacch and Michael B. Shimkin. Cancer **9:** 1073–1074, November-December 1956. (Biometry and Epidemiology Branch, National Cancer Institute, Bethesda, Md.)

Barely a year after their discovery, Edison reported conjunctivitis after a few hours exposure to roentgen rays (Nature, London **53:** 421, 1896). The radiologist's hand became a frequent site of a pigmented dermatitis, of ulcers, and finally of neoplastic changes culminating in distant metastases. Frieben, in 1902, was the first to record a case of cancer associated with exposure to roentgen rays (Fortschr. a. d. Geb. d. Röntgenstrahlen **6:** 106, 1902). By 1911, Krause knew of 54 cases of cancer directly attributable to x-rays (Ztschr. f. Röntgenk. u. Radiumforsch. **13:** 256, 1911).

In 1908, Jean Clunet was prompted to reproduce in white rats the same "sequence of events that seems to occur in those unfortunate colleagues of ours who have become the victims of their radiologic imprudence (Recherches expérimentales sur les tumeurs malignes). The left gluteal and sacral regions of a six-month-old male rat were irradiated cyclically so as to reinduce an ulceration as soon as the previous radiation ulcer had healed. Fourteen months later, at the onset of a fourth cycle of healing, a tumor developed in the zone of scarring. Microscopic examination revealed sarcoma with invasion of muscle. This was the first malignant neoplasm ever to have been induced in an experimental animal.

Radiobiological Effects with 30-MEV Electrons, Preliminary Report. H. R. Schinz and H. Fritz-Niggli. Radiol. clin. **25:** 371–383, November 1956. (In German) (Kantonsspitals Zurich, Zurich, Switzerland)

The authors work with the 31-MEV betatron at Zurich. Removal of the anticathode allows the production of a more or less monochromatic electron beam of 30-MEV energy. The results of various biological tests with such electrons are reported here. Comparison depth-dose curves are given for the betatron roentgen rays, for the betatron electrons, for radiation from the radiocobalt bomb, and for conventional roentgen rays generated at 200 kv.

Criteria for judging biologic effects were mice survivals, *Drosophila* embryo survivals, abnormalities induced in *Drosophila*, etc. No qualitative differences in biological effects were determined between 31-MEV x-rays and the 30-MEV electrons, between 31 MEV x-rays and conventional x-rays, or between 30-MEV electrons and conventional x-rays. There were, however, quantitative differences between the effects of conventional x-rays and the 31-MEV betatron x-rays, the latter being less by a factor of 0.6 to 0.9. Similar differences were found in a comparison of the 30-MEV betatron electrons and conventional x-rays.

Nine figures; 4 tables.

CHRISTIAN V. CIMMINO, M.D.
Fredericksburg, Va.

Cell Division and Nucleic Acid Synthesis in the Regenerating Liver of the Rat. Donald B. Cater, Barbara E. Holmes, and Lorna K. Mee. Acta radiol. **46:** 655–667, November 1956. (Department of Radiotherapeutics, University of Cambridge, Cambridge, England)

After partial hepatectomy in the rat, the liver lobes which remain enter a phase of regeneration and repair. If histologic studies are performed early in this regenerative period, it is possible to observe separately certain processes of cell growth. In this investigation, studies were performed following x-ray irradiation of the liver, after injections of radioactive phosphorus, and after colchicine injections.

Since phosphorus is taken up and utilized in DNA (desoxyribonucleic acid) synthesis, P^{32} injections and counts permitted assessment of the DNA synthesis rate. Direct mitotic counts made at different times provided information regarding mitotic activity.

Colchicine injections and liver irradiation were done to determine their effects on nucleic acid synthesis and mitotic activity, and also to measure the duration of mitosis.

It was found that DNA synthesis, which normally is low in the rat liver, climbs to a peak of about ten times normal activity at approximately twenty-four hours

after partial hepatectomy. At about twenty-seven hours, mitotic activity reaches its peak. Mitosis lasts about one hour.

Irradiation of the liver after partial hepatectomy produces a prompt inhibitory effect upon mitotic activity, but only a delayed effect upon DNA synthesis. The phase of mitosis at the time of irradiation seems essentially unimportant. The effect which radiation has upon mitosis appears to be mediated through some process other than nucleic acid synthesis.

Fourteen diagrams. DON E. MATTHIESEN, M.D.
Phoenix, Ariz.

Effect of *in Vitro* X Irradiation on Pigmented and Pale Slices of Cloudman S91 Mouse Melanoma as Measured by Subsequent Proliferation *in Vivo*. Jewel Plummer Cobb. J. Nat. Cancer Inst. **17:** 657–666, November 1956. (Department of Surgery, New York University Post-Graduate Medical School, New York)

The author's observations are summarized as follows:

"1. The *in vitro* irradiation of pigmented and pale slices of the Cloudman S91 mouse melanoma with 2,500, 2,800, or 3,000 r revealed that a larger number of the pigmented slices remained viable following treatment. Viability was measured by the number of irradiated implants growing successfully in DBA mice, the strain of tumor origin.

"2. A dose of 3,000 r was sufficient to prevent subsequent growth *in vivo* of pale melanoma tissue slices. A dose of 3,500 r was sufficient to prevent subsequent growth *in vivo* of pigmented slices but did not prevent growth in tissue culture. This dose may be regarded as the attenuating dose for pigmented melanoma slices.

"3. Pigmented and pale melanoma slices which survived irradiation and grew in host mice did not lose their capacity to undergo mitosis and to form new melanin. These tumors were similar, histologically, to control tumors.

"4. Counts of cells containing melanin and mitotic-index values for a series of pigmented and pale areas of 8 tumor specimens were evaluated. In pigmented tissue there were consistently more melanized cells per volume of tissue than in pale tissue. Mitotic-index values, on the other hand, followed no consistent pattern in relation to pigmentation areas.

"5. The relatively greater radioresistance *in vitro* of pigmented, as compared to pale, tissue was accompanied by an increased number of melanized cells. An explanation for this phenomenon is discussed."

One graph; 3 tables.

Methods of Estimating Protective Wall Thickness for High Energy Teletherapy Units. Leonard T. Pockman. Radiation Res. **5:** 542–557, November 1956. (Stanford University School of Medicine, San Francisco, Calif.)

Single scattering from a Masonite phantom was calculated by means of the Klein-Nishina formula. Comparison of the results with the measurements of others on the total scattering of Co^{60} gamma rays by a Masonite phantom in the angular range 45° to 110° has made possible a conservative extrapolation for the total scattering to much higher MEV for this same angular range and for 18°. Although these estimates of scattering apply directly only to monochromatic radiation, an approximate method of applying them to the continuous bremsstrahlung from the thin target of a linear accelerator is developed.

For a given or assumed flux of x-rays incident on the phantom, it is shown how the scattered radiation in milliroentgens per hour at 1 meter from the phantom can be calculated for the angular range 45° to 110° and at 18°. This scattered radiation is divided for convenience into monochromatic components. This, together with the inverse-square law and the concrete attentuation curves and coefficients of the National Bureau of Standards and of the Atomic Energy Commission, makes it possible to determine the proper protective wall thickness in the angular range 18° to 180°. In the forward direction (0 ± 7.5°) the thickness of protective concrete barriers to handle the direct beam can be obtained almost directly from *Handbook 55* of the National Bureau of Standards. For the angular range between 7.5° and 18°, the thickness adequate for the forward range will be sufficient. For the angular range 110° to 180°, the thickness calculated for 110° will be adequate. AUTHOR'S ABSTRACT

An Investigation of the Bragg-Gray Principle with Fluorescent X Rays. H. V. Larson. Radiation Res. **5:** 558–568, November 1956. (General Electric Co., Richland, Wash.)

The Bragg-Gray principle was investigated in the energy range from 8.16 to 34.3 Kev for copper- and aluminum-walled Bragg-Gray chambers. Fluorescent x-rays provided nearly monoenergetic photons. The pressure (P) of the air inside the Bragg-Gray chamber was varied, and the corresponding current per gram of air (J_z) was measured. These values were divided by the current per gram of air (J_{air}) as measured with a free-air ionization chamber. A plot of J_z/J_{air} *vs.* P was extrapolated to zero pressure. The Bragg-Gray chamber theory predicts that the limiting value of J_z/J_{air} is proportional to the ratio of the mass energy absorption coefficients (μ^a_z/μ^a_{air}) and inversely proportional to the ratio of the stopping powers $\left(\overline{\frac{dE}{\rho dx}}\right)_z / \left(\overline{\frac{dE}{\rho dx}}\right)_{air}$. The experimental values of J_z/J_{air} agreed within experimental error with the values of J_z/J_{air} that were computed from the known values of the absorption coefficients and stopping powers at 8.16, 16.1, and 23.7 Kev for both the copper and aluminum-walled Bragg-Gray chambers. At 34.3 Kev there is a 15 to 18 per cent difference between the experimental and theoretical values of J_z/J_{air}.

A Comparison of Local and Systemic Effects Following Contact and Flash Burns. James W. Brooks, B. W. Haynes, Jr., W. T. Ham, Jr., Fred Schmidt, and Ray Williams. Ann. Surg. **144:** 768–777, October 1956. (J. W. B., Medical College of Virginia, Richmond, Va.)

Thermal injuries resulting from exposure of the skin to the flash of an atomic detonation are physically somewhat different from burns due to contact with burning clothing, hot water, etc. The effects of simultaneous total-body exposure to sublethal doses of ionizing irradiation further affect the healing response. To promote better understanding of these processes, the authors report their studies upon more than 100 dogs. Since simultaneous exposure to ionizing and thermal radiation, such as occurs during an atomic explosion, could not be achieved in the laboratory, the animals were first burned and then exposed to x-rays, or vice versa. Observations were also made on animals receiving flash burns alone and on a group submitted

only to irradiation. Comparisons are made with previous similar studies on contact burns.

It was clear that flash burns made the animals less ill clinically than did contact burns. The flash evidently caused immediate vaporization of moisture present in the skin, and this led to formation of a firm, leathery eschar fixed to the underlying tissues. This evidently limited the development of local wound infection. Healing was more rapid than with contact burns.

Blood volume and plasma changes seemed similar for both types of injury. The peripheral blood pictures also were parallel in the two types of injury. Blood and wound cultures showed a lower incidence of blood stream infection with flash burns, which, again, was possibly related to the initial eschar formation.

In unburned dogs, 100 r of total body irradiation produced no apparent clinical ill effects. However, white cell counts fell 30 to 40 per cent below controls between six and twenty-four days. Return to normal was attained by the fortieth day. For dogs which were given flash burns plus 100 r whole body irradiation, the mortality was 37 per cent, with death occurring at five or six days. In the other dogs, wound healing was apparently unaffected by the added insult of irradiation. Blood volume and peripheral counts showed that a longer time was required for return to normal than in the unirradiated animals.

Addition of pencillin therapy after flash burn and irradiation seemed to make all phases of the reactions less severe, with uncomplicated recovery.

The authors feel that if thermal dose is constant, a decreased exposure time causes a more severe flash burn lesion. Whether or not irradiation has been superimposed, the general therapeutic approach to either contact or flash injuries will be the same.

Six photomicrographs; 1 photograph; 4 graphs.

DON E. MATTHIESEN, M.D.
Phoenix, Ariz.

Inhalation and Retention of Simulated Radioactive Fall-Out by Mice. I. Study of a Simulant of Fall-Out from Nuclear Detonation Under Sea Water. Stanton H. Cohn, William B. Lane, Joseph K. Gong, John C. Sherwin, and Walter L. Milne. Arch. Indust. Health 14: 333–340, October 1956. (U. S. Naval Radiological Defense Laboratory, San Francisco, Calif.)

The uptake, distribution, and retention of fission products in mice subjected to an acute inhalation exposure from fall-out simulant were investigated. The simulant, first of a series to be studied, contained the ionic form of three-day-old fission products from bombarded uranium. The fission-product mixture, developed in an attempt to represent the fall-out produced by a nuclear detonation in sea water, was aspirated as a liquid aerosol into three animal chambers, at three different concentrations simultaneously, for a period up to one hour.

Examination of the animals one hour after exposure showed the bulk of activity in the gastrointestinal tract, lungs, and head, with smaller amounts in the skeletal system, liver, and blood. A smaller, but a still significant, amount was present in the thyroid. The concentration in the gastrointestinal tract was three times that found in the respiratory tract and lung at this time. At one month following exposure, the skeleton showed the highest residual activity of any tissue, followed by the lungs and head. Barely detectable amounts of activity were present in the liver. At two months activity was still detectable in the skeleton and lungs.

The activity per gram of tissue at one hour following exposure was highest in the respiratory system and thyroid and lowest in the skeleton and liver. Although the gastrointestinal tract contained the largest amount of activity at this time, the total dose it received was the lowest of any of the tissues, due to the rapid biological loss of simulant material by excretion.

The amount of internal contamination taken up by the animals as a result of an acute exposure of one hour was proportional to the length of exposure and to the concentration of air-borne radioactivity. The relatively short biological and radioactive half-life of the inhaled fission products minimizes the internal radiation hazard relative to the external radiation hazard following an acute inhalation exposure to fall-out.

Five figures.

Modification of X-Ray Injury to *Hydra littoralis* by Post-Irradiation Treatment with Magnesium Sulfate and Glutathione. Helen D. Park. Biol. Bull. 111: 240–247, October 1956. (National Institute of Arthritis and Metabolic Diseases, U. S. Department of Health, Education, and Welfare, Bethesda, Md.)

In order to compare the protective effect of glutathione with that of magnesium sulfate, hydras were left in solutions of standard saline, $MgSO_4$, glutathione, and $MgSO_4$ plus glutathione, for twenty-four hours after exposure to 25,000 r x-rays. Non-irradiated controls were also treated with the four solutions; none of these animals died. All of the irradiated groups showed significantly fewer survivors than their controls. The only statistical significant differences among the irradiated groups were between the hydras in $MgSO_4$ and those in saline, and between those in $MgSO_4$ and those in glutathione. There was not sufficient evidence to assert definitely that either the glutathione or the combined treatment had a protective action against the radiation.

The effects of continuous exposure to $MgSO_4$ and glutathione on budding, following irradiation of 4,500 r, were studied. This radiation dose the author had previously found to be approximately one-third that necessary to inhibit bud protection completely for ten days. The rates of budding in each solution were determined. It was found that 4,500 r inhibited the budding of hydras significantly. $MgSO_4$ and $MgSO_4$ plus glutathione stimulated budding of non-irradiated hydras while glutathione alone did not. $MgSO_4$ alone did not significantly modify the inhibitory effect of the radiation on budding. Glutathione alone partially reversed the inhibitory effects of the x-rays. Within a fairly wide range of concentrations of $MgSO_4$ and glutathione, the two agents together restored the budding rate of irradiated hydras to that of the non-irradiated animals in standard saline.

One figure; 2 tables.

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